pp. 377-472] May, 1948

TROPICAL DISEASES BULLETIN

VOL. 45] 1948 [No. 5

MAIN CONTENTS:

	PAGES
Chlorination and Viability of *E. histolytica* Cysts	377–381
Summary of Recent Abstracts. IV. Trypanosomiasis	381–386
Rabies	387–388
Malaria	388–410
Trypanosomiasis	410–418
Leishmaniasis	418–419
Fevers of the Typhus Group	419–424
Yellow Fever	424–425
Plague	425–426
Cholera	426–428
Amoebiasis and Intestinal Protozoal Infections	428–430
Relapsing Fever and other Spirochaetoses	431–436
Leprosy	436–443
Helminthiasis	443–458
Deficiency Diseases	458–460
Sprue	460–462
Haematology	462–463
Venoms and Antivenenes	463–464
Dermatology and Fungus Diseases	464–468
Miscellaneous Diseases	468–469
Protozoology: General	469–470
Entomology and Insecticides: General	470–471
Reports, Surveys and Miscellaneous Papers	471–472

For detailed Contents see pp. ii, iv, vi, viii and x

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BUREAU OF HYGIENE AND TROPICAL DISEASES

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CHLORINATION AND VIABILITY OF *Entamoeba histolytica* CYSTS

By T. C. St. C. Morton, O.B.E., M.D., F.R.C.P., D.T.M. & H., K.H.P.
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Interest in the prevention and cure of amoebiasis was stimulated after the 1914–18 and 1939–45 world wars alike. The only real advance in treatment during the recent war was the introduction of penicillin and sulphaguanidine to counteract the secondary bacterial infection of the gut. Control of the disease has not received adequate attention, probably because of the divergent views of recognized authorities on the mode of transmission. Some emphasize the rôle of water-borne infection and others stress the direct contamination of food and drink by cyst carriers. However, it is agreed that flies play an important secondary rôle as vectors between fresh human faeces and food, but the degree of importance must vary with the humidity because the higher the humidity, the greater the viability of the cysts.

Andrews (1934) has shown that in volunteers who scraped their fingers through faeces containing cysts, the maximum viability of the cysts was 45 minutes in those with long finger nails, and only 15 minutes in those with short. If this fact is confirmed, the food handler is only likely to remain infective for about an hour after defaecation. The routine use of soap, water and a nailbrush could reduce the time still further, and indeed completely neutralize this source of infection.

Sources of Infection

Fresh fruit and salads which are eaten uncooked, such as grapes, lettuces, radishes etc., have deservedly acquired an evil reputation as sources of infection. Unfortunately, the time-honoured measures advocated to render them " safe " to eat savour more of a magical rite than an effective hygienic measure. Potassium permanganate achieved its reputation as a panacea because it was effective in killing the cholera vibrio in a dilution of 1/500,000 in fifteen minutes (Napier, 1945), but even a 1 per cent. solution of potassium permanganate is not effective against the cysts of *E. histolytica* after twenty-four hours' immersion (Craig, 1944). Recent work indicates that after thorough washing to rid the fruit or vegetables of gross organic matter, immersion in a strong solution of bleach for half an hour should render them reasonably safe.

Viability of Entamoeba histolytica *Cysts*

Survival.—The length of survival of cysts is a subject of fundamental importance from the public health point of view, but it was only when cultural methods were introduced that a reliable method of testing for viability became

available. YORKE and ADAMS (1926), found that cysts in faeces always perished at room temperature within nine days. Washed cysts, in concentrated preparations in water, survived for seventeen days at 0°C. and for ten days at 16–20°C. CHANG and FAIR (1940) found that cysts survived in water for ninety days at 32°F. but only for 3 days at 86°F. STONE (quoted by CRAIG, 1944) states that cysts from cultures were still viable after fourteen months at 32°F.

Thermal Death Point.—YORKE and ADAMS (1926), using the culture viability test, found that the thermal death point was 50°C. (122°F.). Cysts survived for thirty minutes at 45°C. but under similar conditions were killed in five minutes at 50°C. CRAIG (1944) recommends immersion of fruit and lettuces, obtained from unsafe sources, for thirty seconds in boiling water. After being treated in this manner, the fruits or vegetables may be freshened by placing them in the ice-box or by immersion in ice-cold boiled water.

Chlorination.—In 1917, WENYON and O'CONNOR stated that cysts of *E. histolytica* could resist free chlorine in water, to a strength of 1 : 10,000, for some hours. Eosin staining was used as the criterion of death, but the fallacy of such a standard was demonstrated by CHANG (1940), who showed that cysts were found to be non-viable by the culture method even when 40–70 per cent. of them failed to take the stain. In 1944 Chang demonstrated further that even when cysts were kept at between 40° and 50°C. for four to five months after death, between 30 and 40 per cent. of them failed to be stained with eosin. He postulated that while the nuclei of the cysts were no longer viable, the cyst wall might resist the infusion of dye for a long time. YORKE and ADAMS (1926), by means of cultural methods, found that cysts were killed in thirty minutes in water containing free chlorine in a strength of about 100 parts per million at laboratory temperatures of between 20° and 25°C. They found that with 21 parts per million of free chlorine under the same conditions, scanty cysts survived. LIU (1928), also using culture methods, stated that with 5,000 parts per million of free chlorine, a contact period of six hours was required to kill all the cysts. SPECTOR, BAYLIS and GULLANS (1934), using eosin staining as a criterion of death, found that cysts were not all killed by an initial dose of chlorine of 500 parts per million in a contact period of 48 hours. These authors also stated that chlorine was more effective than chloramines in killing cysts. GARCIA (1935), based his conclusions on the unproved assumption that cysts showing disappearance of nuclei or broken nuclei and disappearance of karyosomes were dead, and that those showing only distortion of nuclei and disappearance of karyosomes were alive ; on this basis, he stated that cysts in a thick fresh faecal suspension were killed in 1¼ hours with an initial dose of chlorine of 3·5 parts per million, while 3,500 parts per million of free chlorine were required to kill the washed cysts in the same contact period. (In the author's case, a dilution of $CaOCl_2$ of 1/100,000, expressed as chlorine, was equal to 3·5 parts per million, the available chlorine present being 35 per cent.) He concluded that the killing power of chlorine is tremendously increased in the presence of large amounts of organic material, when chloramines are formed. STONE (1937), on the other hand, reported that cysts of *E. histolytica* were not more resistant than *Bact. coli* to chlorine in tap water. He found that in tap water with a density of 1,975 cysts per cc. and a total organic nitrogen content of 45 parts per million, an initial dose of 4 parts per million of free chlorine killed all cysts and *Bact. coli* in twenty minutes. When the total organic nitrogen was increased to 101·25 parts per million, 10 parts per million of free chlorine were required. Cyst suspensions from washed cultures were used, and for tests of viability both eosin staining and culture methods were employed. BRADY, JONES and NEWTON (1943), using raw surface water to which 20 cysts per cmm. were added, found that with an initial dose

of 2·73 parts per million of free chlorine, cysts were still viable at the end of thirty minutes; but by multiplying the dose 2 to 10 times, only 8 cultures were positive out of 640. Of 150 cultures exposed for over 15 minutes to fifteen times the dose, none was positive for *E. histolytica*. In the positive cultures obtained after exposures of twenty minutes or more to concentrations of 2·73 to 9·83 parts per million of chlorine, the frequency of positives was haphazard and bore no relation to the amount of the dose of applied chlorine, nor to the duration of the exposure. A possible explanation for this phenomenon is that a few cysts were protected from the action of the chlorine by particles of organic matter which exerted a dechlorinating effect in small localized areas; such a phenomenon was observed by REGAN (1942) in the case of *Bact. coli* in polluted tidal waters. If such circumstance is of common occurrence, occasional survival of a few cysts may be expected under field conditions unless the water is filtered before chlorination.

CHANG and FAIR (1941), using cysts from cultures and testing viability by cultural methods, evaluated the cysticidal effect of chlorine in terms of temperature, density of cysts and *p*H. They found that the higher the temperature, the lower the *p*H value and the longer the contact period, the greater the cysticidal effect. Doubling the density of the cysts necessitated the use of a 25 per cent. higher concentration of chlorine.

CHANG (1944), with a concentration of 40 washed cysts per cc. and working with gaseous chlorine, an aqueous solution of chlorine, and with chloramines, carried out a very elaborate series of experiments in which the strengths of the stock solutions and of the residual chlorine were determined by the acid-starch iodide method. The *p*H of the chlorinated water was estimated by an electrometer and in the expectation that the oxidation-reduction potentials of the chlorinated water might show a close relation between the concentration of chlorine and the cysticidal efficiency, the voltage of the chlorinated water was determined by a brilliant platinum electrode against calomel half cell. All experiments were carried out at 18°C. and nitrogenous organic matter from domestic sewage and from proteose peptone was used in varying amounts in a parallel series of experiments. In addition, studies were made to find out whether there was a penetration of chlorine into the cysts and what sort of morphological changes took place in them after chlorination. He found that with a high concentration of chlorine, such as 50 parts per million, 65–75 per cent. of the cysts were stained yellow with orthotolidine, and that these yellow-stained forms were coarsely granular. He found that the cysticidal activity of solutions of chlorine, or of chloramines, is associated with the entrance of free chlorine into the cysts. The coarsely granular appearance of cysts was thought to indicate that chlorine probably combined with the proteins in the protoplasm and rendered the latter insoluble. However, in most of the tests made, the cysts were usually killed long before the chlorine was detectable in them, and before the gross changes in appearance had taken place. In several tests it was found that the death of cysts was associated with morphological changes of the nuclei. The earliest changes were splitting of the karyosome and irregularity of the nuclear membrane followed by fading or disappearance of the karyosome and a broken or disintegrating nuclear membrane. The most advanced stage was a total disappearance of the nuclei with irregular granules scattered in the cyst. It was apparent that the death of a cyst was brought about by the destruction of the nuclei, the first sign of which might be the splitting of the karyosome. This, according to Chang, showed that the criterion for viable and non-viable cysts which GARCIA (1935) had postulated, on the basis of the morphological changes seen after chlorination, was not justified. The viability of chlorinated cysts was determined by culture methods. The cysts in each bottle were recovered by centrifugation and were placed in a

tube of liver infusion agar medium which had already been seeded with the bacterial flora isolated from a culture of the N.R.S. strain of *E. histolytica*. Chang suggests that the death of a cyst is the result of the destruction of its nucleus by chlorine ; that the destruction of nucleus depends on the penetration of the chlorine into the cyst ; that the penetration of chlorine into the cyst depends on the nature of the chlorine compound ; and that the amount of active or free chlorine in the water depends on the hydrogen ion concentration of, and the amount of organic matter and ammonia present in, the water, and also on the temperature of the water. The oxidation-reduction potential seems to give a more accurate measurement of the cysticidal or germicidal efficiency of chlorine, since it indicates the amount of active or "free" chlorine present under all conditions.

Chang found that, at a *p*H of 7 and a temperature of 18°C., gaseous chlorine applied for 15–30 minutes is the most powerful cysticidal agent ; hypochlorite is slightly less so and chloramine the least. For long contact periods, such as 120 minutes, the efficiency of all three was about the same.

In another series of experiments, he showed that with a *p*H of 7 at a temperature of 18°C., and with a total organic nitrogen content of 0·1 to 0·19 parts per million, an initial free chlorine of 3 parts per million was effective ; on raising the *p*H to 8·5, 11 parts per million were required to kill all cysts in 30 minutes' exposure.

Summary

The results obtained by different investigators are divergent and contradictory. On critical examination it is obvious that this divergence is due to two factors : different criteria for assessing the viability of the cysts after treatment with chlorine ; and the different conditions, chemical, physical and biological (such as the density of cyst suspensions) under which the tests were made.

(*a*) *Viability*.—The early workers used eosin staining as a criterion of the death of cysts. Chang and Fair (1941) showed this method to be very unreliable. Cysts were found to be non-viable by culture, although 40–70 per cent. failed to take the stain : cysts were kept at 40°–50°F. for four to five months after the period of viability as shown by culture and some 30 to 40 per cent. failed to be stained by eosin. The authors concluded that, while the nuclei of the cysts were no longer viable the cyst wall may resist staining by eosin for a long time. Similarly, the morphological appearance of cysts after chlorination cannot be entirely relied upon as an index of viability. Culture methods, provided adequate controls are used, remain the only practical criterion for viability.

(*b*) *Varying conditions under which the experiments were performed*.—Much of the work of the early investigators is vitiated by the facts that few of them defined the conditions under which these tests were made and that they did not take into account the importance of the temperature, hydrogen ion concentration, density of cyst suspensions and amount of organic matter present in the water.

Conclusions

Under ideal conditions, as little as four parts per million of free chlorine will destroy the cysts of *Entamoeba histolytica* in water after thirty minutes. The presence of organic matter, and its varying nature under field conditions, preclude sole dependence on the cysticidal properties of chlorination. This is taken into account in the sterilization of water in the service water carts, where both filtration and chlorination are carried out.

Potassium permanganate, as a means of "sterilizing" fresh fruit, lettuces, etc., should be abandoned and replaced by strong solutions of bleaching powder containing at least 100–200 parts of free chlorine per million. Subsequent washing should then be done with safe water.

A level teaspoonful of good bleaching powder added to a gallon of water makes approximately a strength of 100 parts per million of free chlorine.

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SUMMARY OF RECENT ABSTRACTS*

IV. TRYPANOSOMIASIS

AFRICAN TRYPANOSOMIASIS

Aetiology

FAIRBAIRN and BURTT (p. 506) have studied the infectivity to man of a strain of *Trypanosoma rhodesiense* isolated in 1934 by CORSON and maintained by cyclical transmission through *Glossina morsitans*, mainly in sheep and antelopes. It is still highly infective to man and shows no sign of reverting to a *T. brucei* type. The authors have noted the fact that a fly may fail to infect a volunteer at one bite, but succeed later, or that the volunteer may be infected by one fly, but not by another, both infected from the same source. They think that the explanation of these anomalies lies in the dose of metacyclic trypanosomes ejected by the fly, and after counting trypanosomes ejected by flies attempting to feed, conclude that the minimum infecting dose for this strain is about 350 trypanosomes. The power of a strain to invade the salivary glands, and its virulence, are also factors, and the authors discuss these. Virulence and infectivity to man are separate and independent, variable qualities. The authors discuss the changes in infectivity to man that may be brought about by prolonged residence in sheep, and changes in virulence which are probably the result of mutation of genes. In comment, Corson suggests that the authors' views on the size of an infective dose may not be accepted unreservedly by some workers, and that there may be a factor of selection working on a heterogeneous strain.

In a long and closely reasoned paper, FAIRBAIRN and CULWICK (p. 649) set out their views on the electrical charges of trypanosomes and the effect of these charges (positive and negative in different individual trypanosomes) on

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1947, v. 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

attraction to or repulsion from other trypanosomes or red blood cells, themselves charged. The authors describe long, short and intermediate forms, and report observations which indicate that syngamy occurs, trypanosomes with opposite electrical charges fusing and later dividing. This process results in a heterogeneous population. BROOM adds a comment to his abstract of this paper ; the whole subject should be studied in the original.

The same authors (p. 1051) show that a sub-strain of *T. rhodesiense*, maintained by cyclical passage through tsetse and sheep, remained polymorphic for 12 years, whereas another substrain, maintained (in England) by syringe passage through mice, has become monomorphic. They argue that it is known that syringe-transmitted strains of the *brucei* group tend to become more sensitive to arsenicals, and that any chemotherapeutic tests should be carried out on strains which are polymorphic and which have been, and are, transmitted by *Glossina*.

LEWIS and LANGRIDGE (p. 980) have studied the trypanosomes (*T. brucei*) ejected by tsetse flies from time to time after infection, and describe the course of development which these appearances suggest that the trypanosomes undergo in the flies. Details should be sought in the original.

WEINMAN (p. 1051) describes a new medium of agar and human citrated plasma and red cells, for the cultivation of *T. gambiense* and *T. rhodesiense*.

Transmission

SCHWETZ (p. 508) discusses the distribution of species of *Glossina* in West Africa ; he thinks that this is not wholly regulated by climate and vegetation.

BEQUAERT (p. 294) describes the tsetse flies of Liberia. There are 4 known species, of which only one, *G. palpalis*, is a vector of human trypanosomes. He advises on measures to control these flies by recognized methods. FERREIRA (p. 1052) contributes a note on the biology of *G. palpalis* in Portuguese Guinea, which is a confirmation of work done elsewhere.

JACKSON (p. 47) allowed *G. morsitans* to hatch from pupae in part of Tanganyika Territory in which this species does not occur, and studied the flies subsequently caught. Most of these were males, and most of them had fed by the fourth day. There is good correlation between age and fraying of the wings. The average distance from the point of hatching, at which the flies were caught, was nearly 400 yards in the first week to nearly 1,000 yards in the fourth, though some were found more than 2,000 yards away. Second generation flies were found, showing that mating had taken place. BURTT (p. 803) has previously shown that *G. morsitans* hatched from pupae incubated at 30°C. are more effective vectors than those from pupae kept at laboratory temperature, but he now notes that this laboratory temperature, in East Africa, may reach 30°C. at certain times of the year. The difference is that incubated pupae remain at that temperature, whereas the others reach it only from time to time.

GLASGOW (p. 47) has observed the seasonal abundance of biting flies in Tanganyika Territory, but concludes that none of them is satisfactory as an indicator species to point the way to an understanding of tsetse distribution and activity.

THOMPSON (p. 803) reports a nematode of the *Mermis* type in tsetse flies.

Control : Treatment : Prophylaxis

Three Annual Reports (for 1944–46) of the Sleeping Sickness Service of Nigeria have been reviewed (MCLETCHIE, p. 971). The staff of this Service was reduced to a maintenance basis during the war, but survey and re-survey work was continued, and protective clearing work was done on a considerable scale, so that by 1944 about 400,000 people had been protected by communal effort. Work on the Anchau tsetse-free corridor was continued, on the lines of development of agricultural resources. In the mining areas, examinations of labourers

are made every 6 weeks, and the average incidence each 6 weeks was 0·67 per cent. in 1945; high enough, but much lower than in 1940. The highest rates of infection found in re-surveys in 1946 ranged from 2 to 12 per cent. in individual hamlets in Katsina, with an average of 2·8 per cent. In most parts of this province the figures show very great reduction over those of 1936–37. Trials of pentamidine as a prophylactic are continued, and a report is given on the trial of certain other drugs in treatment.

MORRIS (p. 51) has attempted control of *G. palpalis* and *G. tachinoides* in the Northern Territories of the Gold Coast, by protective and eradicative clearing. Protective clearing, for example where a road crosses a stream, entails total clearing along the water-course; a total clearing for one mile reduces fly by about 90 per cent. Eradicative clearing entails permanent removal of those species of trees and bushes which give shelter to the flies, especially in the dry season. He begins at the head waters of a river system, and eliminates these trees from the whole system, working down-stream. In one area having 250 miles of river, he achieved by this method an almost (but not quite) total elimination of fly, and a great reduction in sleeping sickness and cattle trypanosomiasis, and thus opened the land to re-settlement.

VANDERPLANK (p. 804) has shown that DDT is lethal to all species of *Glossina* but that when it is applied to cattle, or to screens, its effect is greatly reduced within a few days because the crystals are brushed off by vegetation or washed away by rain. In tests with mosquitoes and tsetse flies, BARLOW and HADAWAY (p. 1053) have found that DDT and gamma benzene hexachloride are absorbed into leaves to the extent of 20–50 per cent.; that on mud walls aqueous suspensions leave more effective films than solutions or emulsions; and that limewash interferes with insecticidal action, largely by physical absorption or masking of the particles. A "sticker" (sulphite lye) also masks the activity of DDT, presumably by coating the particles.

FINDLAY *et al.* (p. 406) have found some repellent action for tsetse flies in four substances, which they name.

VEATCH (p. 293) reports on surveys made in West Liberia in 1941–43, when 90,980 persons were examined and 13,481 cases diagnosed, and again in 1943 in N.W. Liberia, where 32,617 persons were examined, and 2·2 per cent. found infected. Much of the second area had been surveyed in the first expedition. Men were affected more often than women, and the common age incidence was 20–40 years; only 6 per cent. showed infection of the nervous system. Details of treatment with antrypol and tryparsamide are given; good results were achieved.

VAN HOOF (p. 1048) describes the trypanosomiasis campaigns in the Belgian Congo, where each year between 2 million and 5 million people are examined, and infected persons treated. The proportion of infected has remained constant for 10 years at about 0·25 per cent., and there are general reports of an increase in cases resistant to arsenicals, in some places reaching 50 per cent. The recent trend has therefore been to give more attention to prophylactic injections of pentamidine, which protects for 6 months. Arsenic-resistance probably exists in most mixed strains of *T. gambiense* and the resistant strains are selected and eventually predominate as a result of mass treatment with arsenicals. But resistant strains are not so easily transmitted as normal strains by flies [see also PÉLLISSIER below]. The author thinks that malarsen oxide is useful for the treatment of patients with resistant strains (a conclusion not shared by LOURIE). Dogs, pigs and goats can be infected with *T. gambiense*, and may play some part as reservoir hosts in nature. The author failed to infect man with *T. brucei* by the bite of infected flies. He found that immunity to *T. gambiense* is of short duration in animals cured of the infection, but that there

is evidence of cross immunity between *T. gambiense*, *T. rhodesiense* and *T. brucei*, but not between these and *T. congolense*.

Owing to the difficulty of completing the usual course of 12 injections of tryparsamide, at intervals of one week, in patients with *T. gambiense* infection in the Gold Coast, FOWLER (p. 978) has given intensive courses of 2 gm. each day for 6–9 days, either by intravenous drip (lasting 8 hours for each injection) or by ordinary intravenous injections. The results, in a small series of patients, were reasonably good.

PÉLLISSIER (p. 975) discusses tryparsamide in the second stage of *T. gambiense* sleeping sickness, in relation to dosage and to the question of arsenic-resistance. During the war, supplies of tryparsamide were limited, and it was therefore decided that the course should be reduced to 6 injections. The results, as determined by re-survey some four years later, were not good, and a course of 6 doses is consistently less effective than one of 12. Moreover, it has been found that tryparsamide is less effective now than it was in the early days of its use, probably owing to the development of arsenic-resistant strains; there is a tendency to stabilization of results because the arsenic-resistant strains are not so easily transmitted by *Glossina* as the ordinary strains. He also discusses the toxic action of tryparsamide, and the Jarisch-Herxheimer reaction, and the question of arsenic resistance of the patient. EERAERTS (p. 49) gives evidence which suggests that in one area of the Belgian Congo where tryponarsyl had chiefly been used, there had been a considerable development of arsenic resistance. This was later countered by a method of detecting arsenic-resistant strains and treating them with antrypol, tartar emetic and tryparsamide, but the method was difficult. He used antrypol as a prophylactic in the uninfected population, and is enthusiastic as to its value. It apparently cleared an endemic focus.

CECCALDI (p. 45) gives an account of the activities of the Pasteur Institute of Brazzaville in relation to sleeping sickness during 1944. Cases were discovered by mobile units and at fixed dispensaries. Trials were made of *p*-arsenosophenylbutyric acid in treatment, but the results, in general, were not favourable when compared with those achieved by the older remedies. WILLIAMSON and LOURIE (p. 48) have shown that this compound acts on trypanosomes, even if resistant to tryparsamide, but that if *p*-aminobenzoic acid is given *before* the arsenosophenylbutyric acid, the action of the latter is inhibited, probably because the PABA limits its admission into or on to the trypanosome cell. WEINMAN (p. 295) reports on two trivalent arsenical preparations in sleeping sickness in Liberia, namely melarsen oxide and *p*-arsenosophenylbutyric acid. Only a few patients were treated with these drugs.

SCHUELER *et al.* (p. 1052) have used the method of determining the extent to which mapharsen inhibits the utilization of glucose *in vitro* by trypanosomes, as a measure of the anti-trypanosome effect of that drug, and have used strains of *T. equiperdum* of different degrees of arsenic-resistance.

PIERRON (p. 885) claims success in trypanosomiasis by treatment with silver arsenate, but does not give details of the type of infection, or the dosage used.

LEVADITI and VAISMAN (p. 186) confirm old work that fresh rabbit liver extract renders atoxyl trypanocidal *in vitro*, and that glutathione and cysteine have the same effect.

SCHNITZER *et al.* (p. 185) have investigated the rôle of antibodies in the development of drug-resistance by *Trypanosoma equiperdum*. The paper is technical and the subject is complicated; details should be sought in the original.

DE BORCHGRAVE (p. 570) shows that the quinoline derivative "Chinosol" can *in vitro* sterilize blood infected with *T. gambiense*, and that it can be used in

blood transfusion work where there is a possibility that the donor is infected. It shows little activity as a therapeutic agent.

VAN HOOF *et al.* (p. 979) have shown that the protection against *T. gambiense* conferred on guineapigs by injection of pentamidine is not increased by repeated injections of cultures of the trypanosome at intervals after the drug injection, and is therefore presumably independent of specific immunization. They consider that, in proper dosage, this drug may protect man for a period of 6 months, whereas Bayer 205 is said to be active for only 3 months, and is more toxic. They have used pentamidine on a large scale for this purpose, in a dose of 5 mgm. per kilo. CLAESSENS (p. 49) has used propamidine isethionate by intramuscular injection of 5 mgm. per kilo. of body weight, as a prophylactic in the Belgian Congo. Of 131 people so injected, one was found to be newly infected within 6 months. LAUNOY and LAGODSKY (p. 702) find a correlation between the size of protective dose of pentamidine (below toxic level) and the period of protection conferred in rats against subsequent infection with *T. brucei* and other trypanosomes.

Clinical Findings

LAPEYSSONNIE and LAPEYSSONNIE (p. 295) report a case in which trypanosomes [presumably *T. gambiense*] were found in ascitic fluid. In comment, BURKE-GAFFNEY records a similar case seen in East Africa [where the trypanosome was probably *T. rhodesiense*].

HENDERSON-BEGG (p. 509) has found heterophile antibodies in the serum in trypanosomiasis; although in some respects these differ from those found in infectious mononucleosis, care should be taken in diagnosing the latter disease in Africa, on the strength of this test.

COOKSON (p. 975) states that in both trypanosomiasis and leishmaniasis there is excess of serum globulin and euglobulin, and that this can easily be detected by the serum-formalin test. He has used this on sleeping sickness patients and suspects, and although positive results are given in some other conditions, he regards it as a useful ancillary in diagnosis.

Trypanosomiasis of Animals

FULTON and LOURIE (p. 403) have studied immunity in mice infected with *T. congolense* and *T. rhodesiense*, and subsequently treated with phenanthridinium or diamidine compounds. Homologous immunity was marked, with complete failure to reinfect after 20 to 26 weeks respectively; but the immunity sometimes broke down, and this may have been due to changes in the antigenic structure of the trypanosomes as they are passaged. *T. congolense* is antigenically more labile than *T. rhodesiense*, and lability renders the immunization of animals, or man, difficult in the field, where there are many antigenic types.

DAUZIER (p. 805) discusses the immunity associated with drug treatment of certain experimental trypanosome infections. The original paper is a long thesis, and an adequate summary is impossible in a small space.

A study of plasma proteins, erythrocyte sedimentation rate, potassium levels in serum and blood, and fragility of red cells during the course of infection with *T. brucei*, *T. equiperdum* and *T. lewisi* in rats, is reported by IKEJIANI (p. 572), but for details the reader should consult the original.

LAWS (p. 804) find that the method of counting *T. congolense* against leucocytes, in thick films, gives a reasonably accurate measure of the infection in cattle. LAUNOY and PRIEUR (p. 509) show that the two phenanthridinium compounds S.897 and S.1553 are active against *T. congolense*, and can be injected subcutaneously.

VAISMAN (p. 981) reports experiments which indicate that, under certain conditions of infection, *Trep. duttoni* attenuates infection by *Trypanosoma brucei* and *T. equiperdum* in mice.

Chagas's Disease

Torrealba (p. 187) has republished a series of his own papers on Chagas's disease in Venezuela ; most of these have already been reviewed, but together they form an extensive survey of information. Seijas Rivas (p. 297) reports on Chagas's disease in part of Venezuela.

Ponce Caballero (p. 54) found a few cases of Chagas's disease in Bolivia, and remarks that the presence of *T. cruzi* in the blood is transient. Angel Torrico (p. 510) names 35 vertebrate hosts of *T. cruzi* and the 7 commonly infected bugs of Bolivia.

Romaña *et al.* (p. 404) found 23 per cent. of children, in one area of Argentina, positive to Chagas's disease by xeno-diagnosis, and 51 per cent. by complement-fixation test.

d'Andurain (p. 511) found infection in the rodent *Octodon degus degus* in Chile.

Floch (p. 53) in French Guiana infected *Rhodnius pictipes*, *R. prolixus* and *T. rubrofasciata* with *T. cruzi*, the two first more readily than the last. There is evidence that the local strains are more specially adapted to them than to *T. rubrofasciata*.

Hawking (p. 1054) has cultivated *T. cruzi* in tissue cultures of rat embryo cells. Leishmania forms appear in cardiac muscle cells, and eventually complete trypanosomes are formed, which become extra-cellular.

Adler and Bichowsky (p. 52) have found that biotin concentrate inhibits the growth of *T. cruzi* and certain other protozoa, but the active substance in the concentrate is not biotin itself.

Muniz and de Freitas (p. 296) have found that if *T. cruzi* is washed free of all blood constituents before being inoculated into the liquid of fresh N.N.N. medium, the transformation into crithidia forms which usually occurs does not take place. They have investigated the reason. The same authors (p. 571) have prepared an antigen from *T. cruzi* which is a mass of disintegrated culture forms suspended in a saline solution of merthiolate ; this ensures retention of antigenic properties for a considerable time. With this, complement-fixation tests have been performed and correlated with agglutinin and precipitin reactions. The tests revealed fluctuations in the immune state. Immunity shows itself early in infection, when the reticulo-endothelial system is mobilized, and increases as the blood is invaded ; the development of leishmania forms is a defence against this vigorous immunity, for these forms develop into trypanosomes when grown in medium lacking immune bodies. In the body, antibody formation decreases when the leishmania forms predominate.

Romaña and Gil (p. 405) describe the preparation of an antigen for use in the complement-fixation test in Chagas's disease. This test is positive only in that disease with the exception that weak reactions are given in cutaneous leishmaniasis. The authors give details of their results.

Hauschka *et al.* (p. 1054) have shown that infection with *T. cruzi* significantly retards the growth of certain tumours in mice.

Earle (p. 53) reports a case of Chagas's disease which cleared up, apparently, as a result of intravenous administration of penicillin.

Charles Wilcocks

RABIES

REMLINGER, P. & BAILLY, J. La rage. Etudes cliniques, expérimentales et immunologiques. [**Rabies : Clinical, Experimental and Immunological Studies.**] pp. v+192. [Bibliography.] 1947. Paris: Librairie Maloine, 27 rue de l'École-de-Médecine. [18*s*. 6*d*.]

The volume under review summarizes 320 studies on rabies made between 1903 and 1946 by Remlinger and his collaborators. Of these studies, 169 are by Remlinger, 4 by Bailly, 135 conjointly, and 12 by one or other of the authors assisted by LEGER, TEPPAZ, BEL, CURASSON or MICHEL.

Although it is in no sense a textbook on rabies, nevertheless, thanks to the authors' admirable arrangement of the subject matter and to their clear and concise treatment of a majority of the problems likely to face workers in this field, the volume will form a welcome and valuable addition to the reference libraries of anti-rabies institutes.

While it is true that most of the information now presented in so attractive and readable a form will be familiar to the specialist in rabies and its treatment, yet certain of the authors' conclusions and opinions merit special attention and justify recapitulation :

Rabies virus :

Street v. *Fixed Virus*.—The " singleness " of street virus is contrasted with the " plurality " of fixed virus—a virus " fixed " only in name. Proof of " singleness " is afforded by cross-immunity experiments with variously derived street virus strains, including those endowed with hypernormal virulence (" *renforcés* "). Proof of " plurality " of fixed virus is based on the wide variation, ranging from the exclusively paralytic to the purely encephalitic, in the symptomatology of rabies among rabbits used in treatment, particularly as regards the day of death, and on the difference in the resistance of such viruses to attenuating agents and in their pathogenic power for the anterior chamber of the rabbit's eye and for the cellular tissues of man and dog.

The nature of rabies virus.—The hypothesis first advanced by Remlinger in 1918 that rabies is due to a chemical substance of a protein nature, on the frontier between the organic and the inorganic, receives support, by analogy, from the work carried out in 1935 by STANLEY and his colleagues on the virus of the mosaic disease of plants. STANLEY was able to crystallize the latter virus, discovering it to be a macromolecule of protein, reproducing itself apparently by a process of autocatalysis. Such a conception, if somewhat at variance with the more popular microsporidial theory of rabies virus (*Glugea lyssae*, *Encephalitozoon rabiei*), is not wholly irreconcilable therewith.

Anti-rabies treatment.—The " singleness " of street virus obviates the need for polyvalent or autogenous vaccines ; failures of treatment, even in the case of reinforced viruses, are attributable almost entirely to insufficient therapy. Standardization of treatment is a desideratum, to be achieved possibly by providing all anti-rabies institutes with the same strain of fixed virus, one combining a high degree of immunizing power with complete innocuity. Were such standardization to prove acceptable, phenolized killed virus vaccine would bid fair to becoming the product of choice, by virtue of its undoubted efficacy, its keeping properties, the decentralization which its use makes possible and its comparative freedom from neuroparalytic accidents.

A strong plea, founded on the experience of French North African territories, is made not only for canine prophylaxis but also for the treatment of dogs and other domestic animals bitten by rabid animals. For canine prophylaxis, use is made of a 5 per cent. fixed virus rabbit-or dog-brain, in 1 per cent. phenolized water, inactivated at 37°C. ; of this vaccine 40 cc. are administered on the first

day; 24 hours afterwards a further dose of 40 cc. is given. Revaccination annually with 40 cc. is advocated. In the treatment of dogs bitten by rabid animals, 3 to 10 injections, each of 40 cc. of the same vaccine, have been followed by encouraging results. Similarly in the case of horses and cattle, success has attended the exhibition of 40 cc. of the phenolized vaccine on 3 successive days; in severe head bites a further dosage of 40 cc. is administered on the 4th day; a total of 120–180 cc. is advised according to gravity of wounding.

Finally, the need for an international rabies conference, similar to that held in Paris in 1927, is urged. Items on the provisional agenda suggested include: the nature of rabies virus; the influence of rabbit passage on the susceptibility of fixed virus to the action of attenuating agents; the possibility and desirability of standardization of treatment; the neuro-paralytic accidents of treatment; the vaccination of dogs before and after having been bitten; and the vaccination of domestic animals generally. *G. Stuart*

MALARIA

i. SHORTT, H. E. & GARNHAM, P. C. C. **Pre-erythrocytic Stage in Mammalian Malaria Parasites.** [Correspondence.] *Nature.* 1948, Jan. 24, 126.

ii. ——, —— & MALAMOS, B. **The Pre-erythrocytic Stage of Mammalian Malaria.** *Brit. Med. J.* 1948, Jan. 31, 192–4, 4 figs. [14 refs.]

iii. HAWKING, F. **Pre-erythrocytic Stage in Mammalian Malaria Parasites.** [Correspondence.] *Nature.* 1948, Jan. 31, 175.

i & ii. Attempts to discover the developmental forms of sporozoites of *Plasmodium cynomolgi* in the monkey by the Mammalian Malaria Enquiry [this *Bulletin*, 1947, v. 44, 966] working in India, by HUFF and COULSTON in America [*ibid.*, 1945, v. 42, 538] and by others have yielded only negative results. The authors of the present notes have been more fortunate, as they have discovered the pre-erythrocytic stages in two monkeys receiving large doses of sporozoites. Of a batch of *Anopheles maculipennis atroparvus*, fed ten days before on an infected monkey, dissection of 20 showed that all were heavily infected. Accordingly 576 mosquitoes were given the opportunity of feeding on a clean rhesus monkey. Over 500 of the mosquitoes fed. The mosquitoes were then ground in a mortar in 10 cc. of heparinized monkey plasma diluted with normal saline solution. Half the suspension was inoculated intraperitoneally and the other half into the thigh muscles of the same monkey. The suspension showed an average of 5 sporozoites per field of the 1/12″ objective.

The monkey was sacrificed seven days later and a complete examination was made. Though all the tissues have not been thoroughly examined, inspection of the liver sections and smears has revealed what are undoubtedly the pre-erythrocytic developmental forms in the shape of multinucleated plasmodial masses measuring 26 to 30μ in longest diameter and containing 200–300 nuclei. In a number of the schizonts are one or more vacuoles. The extent of infection of the liver is shown by the occurrence of 36 schizonts in a section measuring 90 sq. mm.

Suspensions of liver, spleen, brain, lung, kidney, peritoneal fluid and heart blood were inoculated to clean monkeys which had remained negative for one month at the time of writing. Similar bodies were found in the liver of a second monkey killed on the 6th day after mosquito feeding and injection of sporozoites. In this case the schizonts were smaller and it was possible to determine that the parasites were in the parenchyma cells.

The importance of this discovery lies in the fact that *P. cynomolgi* resembles *P. vivax* of man very closely ; this strengthens the belief that such forms are likely to occur in human malaria.

iii. Hawking, who has been studying the early development of *P. cynomolgi* for some time without success, was shown the preparations of SHORTT, GARNHAM and MALAMOS and returned to his own preparations. In livers of three monkeys which had received sporozoites of *P. cynomolgi* he discovered similar pre-erythrocytic schizonts. One rhesus monkey had been inoculated intravenously and parenterally with the sporozoites from 120 infected mosquitoes. It was killed 7 days, 23 hours later. Large schizonts, 28μ in diameter, were found in the liver ; similar forms were found in the liver of a monkey killed 7 days 15 hours after intravenous injection of the ground-up thoraces of 1,000 infected mosquitoes. A third monkey inoculated intravenously with the suspension of 40 infected mosquitoes was killed 5 days later. Schizonts 14μ in diameter were found in the parenchymatous cells of the liver. Inoculation of emulsion of organs of these monkeys was not followed by infection. *C. M. Wenyon*

BULL. WORLD HEALTH ORGANIZATION (United Nations). 1947/48, v. 1, No. 1, 21–8. **Expert Committee on Malaria.** Extract from the Report on the First Session, Geneva, Palais des Nations, 22–25 April 1947.

The urgent importance of the malaria problem caused the Committee on Epidemiology and Quarantine of the Interim Commission of the W.H.O. to set up an Expert Committee to examine it. This Expert Committee met in Geneva in April 1947, and submitted its report, of which this paper is an extract, in August of the same year.

The Expert Committee formed a natural link with the former Malaria Commission of the League of Nations : but a very different field of work confronted it, for the intervening years had brought about new problems and new solutions, and, indeed, the very conception of the mechanism of malarial infection had itself changed, with the newer discoveries regarding the exoerythrocytic cycle.

The original Report comprises ten sections, a number of which are concerned with administrative questions. The extract under review deals more specifically with certain technical aspects of the problem, notably those relating to suppressive treatment, causal prophylaxis, new synthetic drugs and new means of administration of former ones, and the development of new contact insecticides. All of these subjects have been dealt with fully in this *Bulletin* during recent years. The present paper refers briefly to the successes achieved during and since the recent war in the chemotherapeutic control of malaria and its epidemiological control by means of DDT.

Reference is made to the successful field experiments with atebrin [mepacrine], to the work on the 4-amino-quinolines, sontochin (SN 6911) and chloroquine (SN 7618), the 8-amino-quinolines, such as pentaquine, and the biguanides, of which the most important is paludrine.

The use of DDT as a larvicide and more particularly as a mosquitocide is briefly reviewed. The limitations of its use in the former capacity are noted, and it is pointed out that DDT, especially when used from aeroplanes, may upset the economy and normal biological cycles of a region, from the standpoint of animals, crops and trees.

The value of DDT in destroying the adult vector of malaria is supplemented by its effect on other domestic insects, and it may thus influence indirectly the local morbidity from causes other than malaria.

Large-scale house-spraying with DDT will depend on the budgeting facilities of each country concerned ; the Report discusses the economic aspects of this matter and the Committee emphasizes that the time has come when more

effort should be devoted to developing methods for more practical and economical control of malaria with this powerful weapon. It is pointed out that, to maintain a reduced incidence of diseases after successful control by DDT, the latter will probably have to be used as a recurring measure, and this will require to be taken into account when over-optimistic health authorities are contemplating a budgetary reduction. *H. J. O'D. Burke-Gaffney*

SPADARO, O. Indice splenico ed indice parassitario in gruppi di popolazione araba in arrivo nel porto di Massaua. [**Splenic and Parasitic Indices in a Group of Arab Immigrants in Massawa.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1947, v. 7, Nos. 3/4, 259–61.

The English summary appended to the paper is as follows :—

" The author has searched the splenic index and the parasite index in a group of natives of the Northern Dankalia and of the Yemen who came to Massawa for work. Both groups have given a comparatively low index."

MAUZÉ, J. Contribution à l'étude du paludisme dans les Nouvelles-Hébrides (particulièrement pendant la campagne du Sud-Ouest Pacifique Janvier 1942–Décembre 1943). [**Contribution to the Study of Malaria in the New Hebrides, chiefly during the War in the South-West Pacific, January 1942 to December 1943.**] *Méd. Trop.* Marseilles. 1946, v. 6, No. 2, 109–38, 7 graphs & 1 pl.

There are very scant references in the literature to malaria in the New Hebrides. In collecting material for this report, the author expresses indebtedness to assistance given by colleagues of the United States Forces during their stay in this island group.

The New Hebrides archipelago lies between New Caledonia, in the south, and the Solomon Islands, and about midway between Fiji and the east coast of Queensland. More than 40 of the islands are inhabited : some of these are very small, 120 to 1,200 acres, or even less. The largest island, Espiritu-Santo, covers an area of 5,000 square kilometres. The second largest, Mallicolo, is about half that size. The islands are of both volcanic and coral formation : volcanic activity is manifest in many of the islands. The " kanaka " population probably does not exceed 50,000 ; no census has ever been taken. In addition there are 939 French, English and half-castes, most of whom live in Vale, the capital, in the island of Vaté.

The New Hebrides have always had an evil reputation for malaria. Hospital and dispensary attendances during three recent years show it to be the most prevalent disease : malaria 4,267, pulmonary diseases 2,531, yaws 942, amoebiasis 895, syphilis 502, gonorrhoea 457 and helminthiasis 266. Seven weeks after the installation of a contingent of United States marines in the island of Vaté, 47 per cent. of its strength were incapacitated by malaria.

P. falciparum is the most prevalent parasite, about 75 per cent. of all infections; *P. malariae* about 15 per cent. and *P. vivax* about 10 per cent. Serious clinical forms of malaria are relatively rare.

The only *Anopheles* found in the New Hebrides is *A. punctulatus* var. *moluccensis* [now known as *A. punctulatus farauti*] of which detailed morphological and biological descriptions are given. It is ubiquitous. It has a great variety of breeding places ; in the dry season larvae are found in rivers, streams, springs, irrigated land, seepages and open wells, and in the rainy season in many collections of casual water as well. The water may be clear, turbid, stagnant, saline or almost pure rain water, and with or without vegetation. The only

waters in which larvae have not been found are open surfaces of running water, and water in broken coconut shells and holes in tree trunks.

The New Hebrides mark the southernmost extension of anophelines and malaria in the Pacific : in New Caledonia there are neither.

Norman White

PENIDO, H. M. Alguns aspectos da epidemiologia e contrôle da malária na área do Rio Doce. [**Certain Aspects of the Epidemiology and Control of Malaria in the River Doce Area.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, v. 1, No. 1, 61–76, 1 map & 1 chart. English summary.

In this contribution to the first inter-American Congress of Medicine, the author outlines the malaria problems and malaria control measures applied in 33 townships situated along 660 kilometres of the Vitória-Minas Railway. From Vitória, a coastal town in the State of Espírito Santo, the railway runs north 950 kilometres to reach the River Doce near Barbados. There it turns westward and enters the State of Minas Gerais ; it runs alongside the River Doce to Ipatinga (458 km.). From Ipatinga it runs along the valley of the Piracicaba River, a tributary of the Doce, to Dezembargador Drummond.

The intensity of malaria varies considerably in places along the track from Vitória to Barbados in Espírito Santo. A random sampling of the blood of persons living in 12 places in May of each of four years showed Alfredo Maia to be the most heavily infected, the percentage of positive slides varying from 11 to 30·8. Along the whole railway, *A. darlingi* is the most important vector, the only one except in the first hundred kilometres from Vitória where *A. albitarsis* is also very prevalent. In the neighbourhood of Vitória, *A. aquasalis* also transmits malaria. The oöcyst rate of 781 *A. darlingi* dissected was 7·5 and of 226 *A. albitarsis* 1·3 per cent. The examination of patients attending medical posts along the first 150 miles of track showed that *P. vivax* infections were more numerous than *P. falciparum* infections, except in March and April, the end of the rainy season. *P. malariae* infections were rare.

The first two hundred kilometres of the line up the Doce Valley are practically free from malaria ; the river bed is narrow and confined, but from Derribadinha to Dez. Drummond, 210 km., settlements on the banks of the Doce and Piracicaba Rivers are intensely malarious. Positive findings in samples of blood films taken in the month of May in four consecutive years in 21 localities show the intensity of infection ; in one case the infection rate was 50 per cent. Dispensary records show that in this part of the line also, *P. vivax* exceed *P. falciparum* infections in number except in the rainy months February to May : in April *P. falciparum* infections were more than double those of *P. vivax*.

The rainy season begins at the end of October or early November and 1,500 mm. of rain fall in five or six months. The river overflows its banks and actual and potential breeding places for *A. darlingi* are enormously increased. Antilarval control becomes almost impossible ; epidemic malaria ensues, its severity being determined by the nature of the rainfall. In the dry season, however, antilarval measures have been carried out with success ; chief reliance has been placed on Paris green and small drainage work. The method of work is described.

DDT promises to provide a much more economical method of malaria control in areas that have as low a density of population as has the Doce Valley. A start has been made. An aqueous suspension of DDT has been applied at the rate of 2 gm. per square metre. It is proposed to treat the houses three times a year. [For details of control measures used, see BRAGA *et al.* below p. 408.]

Norman White

SCHWETZ, J. Sur le anophèles et le paludisme endémique et epidémique des noirs dans les régions de hautes altitudes de l'Afrique intertropicale. [**The *Anopheles* and the Endemic and Epidemic Malaria of Africans in Elevated Regions of Tropical Africa.**] *Riv. di Malariologia.* 1947, Oct., v. 26, No. 5, 227–33.

This paper is a concise summary of the results of numerous investigations carried out by the author in the Belgian Congo. All the facts have been described in previous publications and have been duly noted in this *Bulletin*. Chief consideration is given to the *Anopheles* and malaria at high altitudes along the eastern frontier of the Belgian Congo [this *Bulletin*, 1947, v. 44, 786].

Norman White

WOLFS, J. Sur la faune culicidienne de l'agglomération de Coquilhatville. (Troisième note.) [**The Mosquitoes in the Coquilhatville Region.**] *Ann. Soc. Belge de Méd. Trop.* 1947, June 30, v. 27, No. 2, 265–71, 1 fig. & 1 chart on pl.

In 1946 the author continued investigations which he had made previously into the breeding places of *Anopheles moucheti* along the banks of the river Congo, but had no success because of the backwash caused by the boats which continually pass up and down the river. In backwaters along the Ruki river, the water was too foul to admit of breeding by this mosquito and so he comes to the conclusion that most of the *A. moucheti* that infest Coquilhatville come from the islands in the river (Congo).

Brief notes on the breeding places of species of *Aëdes* are given and there is a list of 5 species of anophelines and 44 culicines recorded in 1944 and 1945, which shows that the common species are present all the year round.

H. S. Leeson

WANSON, M., WOLFS, J. & LEBIED, B. Comportement de l'*Anopheles* (*Myzomyia*) *moucheti* Evans. [**The Bionomics of *Anopheles moucheti*.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1947, July, No. 6, 39–62, 2 charts. [25 refs.]

This account of the bionomics of *Anopheles moucheti* is the result of observations made at Coquilhatville and at Léopoldville in the Belgian Congo. Data are given and compared with those obtained by other workers at Stanleyville and Yangambi and, where relevant, with those for *A. gambiae*, because though this anopheline is more common in some places at certain times, it is not so common as *A. moucheti* at Coquilhatville. Matters discussed include numerical abundance and seasonal prevalence, types of breeding places and larval requirements, the influence of distance between breeding and feeding places, outdoor and indoor resting places, longevity and feeding habits of the females and their infectivity with the plasmodium of malaria.

For breeding, this mosquito requires fresh water, constantly replenished and shaded; these conditions it finds on the alluvial islands in the river (Congo), and even when the water rises at flood time larvae may be found among dense masses of reeds at the downstream ends of the islands where they are sheltered from the current. Larvae are also to be found among floating vegetation which has broken away from the islands and the river banks. At Léopoldville (Stanley Pool) the islands are not so numerous and the height of the water reduces the number of breeding places, thus limiting the output of adults. In mid-November, about three weeks after the floods have reached their maximum, breeding places are again available and in January the mosquito catches in the prison, which is the nearest catching station to the Pool, yield three times as many *A. moucheti* as *A. gambiae*.

Outside haunts of this anopheline at Coquilhatville are found among trees, in the shade and not far from the breeding places, but they have not yet been discovered at Léopoldville. A study of the feeding habits and the ovarian development of females has shown that the majority found in houses possess ovaries in stages I and II. Typical figures for outdoor catches give 20 per cent. females with ovaries in stage V and 60 per cent. for females which have not fed. In fishermen's huts on the islands, examination of 500 females of *A. moucheti* showed 31 per cent. with stage V ovaries and only 3 per cent. in stage I. Sporozoite rate at Coquilhatville is 0·072 per cent., whereas at the fishermen's huts at Stanley Pool the rate is 6·3 per cent.

From these observations and a great many more, the authors conclude that, *A. moucheti* is short-lived, that the female needs only one blood meal to mature the eggs, that it enters houses, rests for some time before feeding and then leaves immediately to digest the meal and to mature the eggs outside; there is evidence also that the sporozoite index is fairly constant in any one locality, and varies only according to the distance from the breeding places.

In the laboratory, *A. moucheti* has been observed to deposit an average of 200 eggs per female; eggs hatch in 12 to 24 hours and the larval stage lasts 10 to 11 days. The whole life-cycle can be completed in 13 to 14 days and males and females emerge in approximately equal numbers. The authors have not yet succeeded in establishing a laboratory colony. The discovery of a blue coloration infiltrating the thoracic muscles is a matter for future investigation. *H. S. Leeson*

LAUTERBURG-BONJOUR, M. Die Abwehrfunktionen des menschlichen Körpers gegen die Malaria. [**Defensive Functions of the Human Body against Malaria.**] *Schweiz. med. Woch.* 1947, Dec. 27, v. 77, No. 52, 1359–62.

In his discussion of immunity in malaria, the author concludes that it is not a simple process but is very complex. Apart from normal phagocytosis there is a phagocytosis which is stimulated by parasitic and antitoxic substances which have been demonstrated in the blood. The immunity is strongly specific, not only for the kind of malaria but for the particular race of parasite. In endemic areas, a latent malarial infection is of value in that it prevents reinfection with the same race of parasite. Such a latent infection in persons going to new malarial localities is not able to prevent infection with any new race to which there is exposure. *C. M. Wenyon*

BOYD, M. F. & KITCHEN, S. F. **On the Homogeneity or Heterogeneity of *Plasmodium vivax* Infections acquired in highly Endemic Regions.** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 29–34.

It was noticed that some soldiers returning to the U.S.A. from highly endemic areas in the Pacific, developed repeated attacks of *P. vivax* malaria. The intervals between these attacks were usually short, and the febrile episodes were thought to be recrudescences rather than relapses (as defined by BOYD & KITCHEN, this *Bulletin*, 1945, v. 42, 174). The men had been on daily suppressive quinacrine and the malaria did not appear until this therapy was discontinued. The authors considered that several strains of *P. vivax* were acquired and either that all these strains were reactivated simultaneously during the recrudescences or that some strains would recover from the "quinacrine induced lethargy" earlier than the remainder. If the first explanation were correct, the parasites of the various recrudescences should show complete cross immunity. On the other hand, if each recrudescence represented an infection by heterologous strains, then cross immunity should be lacking.

Mental patients were therefore hyper-immunized against one of three strains recovered from a young soldier who had suffered from many attacks of *P. vivax* malaria contracted in the Pacific. The results indicated that two of the strains appeared to be closely allied if not identical, while the third showed a substantial difference. *P. C. C. Garnham*

MAKARI, J. G. **Intradermal Test in Malaria. Parts I, II & III.** *J. Trop. Med. & Hyg.* 1946, Apr.–May & June–July, v. 49, Nos. 2 & 3, 23–9; 47–54, 7 figs. [19 refs.]

The antigen for this test was obtained from the blood of a chicken heavily infected with *P. gallinaceum*. Heart blood was put in small oxalated tubes, 2 cc. in each. Plasma was separated by centrifuge and discarded. The corpuscles were washed four times with saline and then dried *in vacuo*. After 2 months they were transferred to clean test tubes and sealed, and kept at room temperature, about 30°C., for two months. To prepare the stock solution the powder was triturated in a mortar. A suspension of 1 per cent. of this powder in 0·5 per cent. carbolized salt solution was then prepared, and incubated for 24 hours at 37°C.; it was then passed through a Seitz filter and tested for sterility. This sterile fluid was used in the intradermal tests.

In making the test, 0.1 ml. was injected intradermally on the forearm. Readings were taken after 24 hours. The diameter of redness was measured in millimetres and the results were recorded as follows:

0– 4 mm.	0
5– 9 mm.	+
10–14 mm.	++
15–19 mm.	+++
20 mm. and over ...	++++

Of 70 persons with no history of malaria, 63 gave a negative reaction, 5 had a +, and 1 had a ++ reaction.

Of 71 patients who had had malaria 18 months previously, 65 gave a positive intradermal test.

Of 31 others having a history of malaria within 3 years or more, 29 gave a positive test.

The sensitivity of the tissues to the malarial antigen appears to reach its peak from 2 to 5 months after an attack. In the majority of cases it is never lost completely.

II. Another antigen "N" was prepared from normal chicken erythrocytes in the same manner as was the malarial antigen "M" from malaria-infected erythrocytes described above. Antigen "N" gave positive reactions in 14 per cent., antigen "M" in 20 per cent. of 70 boys with no history of malaria. These pseudo-positive reactions were all weak (+). Of the false reactions to antigen "N", 90 per cent. were in individuals of blood groups O or B, in both cases having anti-A antibodies which would react with the A-like Forssman antigen found in normal chicken red cells. Antigen "N" gave weak positive reactions in 40 per cent. of the malarial series; malarial infection stimulates the production of heterophile antibodies. The control testing with normal antigen "N" should always accompany the testing with malarial antigen "M" to eliminate a number of false positive reactions.

III. The author believes that a combined use of the intradermal test and the cephalin cholesterol flocculation test [this *Bulletin*, 1946, v. 43, 623; 1947, v. 44, 279] would assist in the detection of chronic, masked and latent forms of malaria and the determination of the activity of the infection; in assessing the rôle of malaria in determining false positive serological reactions;

in ruling out malaria in the blood plasma programmes ; and in solving problems created by returning malaria carriers from overseas. *Norman White*

MAKARI, J. G. **Altered Tuberculin Sensitivity in Chronic Malaria.** *J. Trop. Med. & Hyg.* 1947, Sept., v. 50, No. 9, 183–5. [11 refs.]

The author has submitted a number of Armenian refugees, in Syria, to the tuberculin test, the intradermal malaria test [see above], and the cephalin-cholesterol flocculation test. There were 58 persons with chronic malaria, and 60 in whom malaria was excluded by negative history and negative intradermal test.

In general, the results indicated that the incidence of positive tuberculin tests (OT, 1 in 1,000) was higher (41·4 per cent.) in those with chronic malaria than in the controls (23·3 per cent.) and that the difference is statistically significant. Moreover, the incidence of positive tuberculin tests appeared to be related to the activity of the malaria, as estimated by the cephalin-cholesterol test, and to the sensitivity of the tissues in response to the malarial antigen.

The author discusses the possibility that there may be a relationship between the proteins of the tubercle bacillus and the malaria parasite ; that the tubercle bacillus may have a predilection for tissues damaged by malaria ; and that persons with chronic infections may react more readily than normal persons to antigens other than those from the organism infecting them.

[The author places a high degree of reliance on the cephalin test, but in a previous paper (this *Bulletin*, 1946, v. 43, 623 ; 1947, v. 44, 279) he claimed accuracy of only 91·4 per cent. for it. It seems likely that the cumulative errors of all these tests might be considerable.] *Charles Wilcocks*

SCHEIFLEY, C. H. **Malaria : a Note on its Latency and Report of a Case.** *Proc. Staff Meetings Mayo Clinic.* 1947, Feb. 5, v. 22, No. 3, 49–52.

" It is commonly thought that a primary attack of malaria may occur a year or more after cessation of suppressive medication. A review of the literature failed to reveal any well-documented reports to bear out this assumption. In the case reported in this paper, benign tertian malaria developed twelve months or more after suppressive therapy had been discontinued."

BOYD, M. F. **A Note on the Chronicity of a Quartan Malaria Infection.** *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 99–101.

" A naturally induced *P. malariae* infection has persisted in a latent chronic condition in a colored patient for a period of 4,305 days, or 11 years, 9 months, 14 days since the original inoculation."

SOYSA, E. **Malarial Episodes. A Clinical Study of Atypical, Pernicious and Lethal Cases selected from among 10,000 Malarial Patients admitted to Military Hospitals in Ceylon.** *J. Roy. Army Med. Corps.* 1947, Nov., v. 89, No. 5, 205–22, 3 figs.

To illustrate the diversity of clinical features that may result from malarial infections the author has selected twelve cases from the 10,000 that were treated in two military hospitals in Ceylon during a period of four years. All the cases present unusual features and are fully and well described. They illustrate apyrexial malaria, hyperpyrexia, algid malaria, cerebral malaria, malaria encephalopathy, malarial neuritis, malarial jaundice, malarial dysentery,

severe malarial anaemia, malarial leucopenia, malarial haemoglobinuria and malarial pneumonia. The nature and length of this interesting paper preclude a summary. *Norman White*

MELLINKOFF, S. M. & HIGGINS, J. R. **The Heart Rate in Malaria ; a Review of Ninety Cases.** *Ann. Intern. Med.* 1947, Sept., v. 27, No. 3, 433–40, 4 figs. [10 refs.]

This paper concerns the heart rate in 90 patients suffering from malaria contracted for the most part in the Philippine Islands. In most cases, the appearance of clinical symptoms had been delayed by the administration of prophylactic doses of atebrin. There were 85 patients with *P. vivax* infections, 2 with *P. falciparum* and 3 with *P. malariae*. The pulse readings record the greatest relative tachycardia observed at the height of each initial fever. After the subsidence of fever and malaise the resting pulse rate was recorded in each case, an hour after the patient had awakened from a good night's sleep, the interval hour having been spent in bed. The results of the study show that malarial fevers may be accompanied by rates of heart beat ranging from tachycardia like that which characterizes many bacterial infections to bradycardia like that of typhoid fever. About one-fourth of these patients had a relative bradycardia. *Norman White*

BOSHES, B. **Neuropsychiatric Manifestations during the Course of Malaria. Experiences in the Mediterranean Theater in World War II.** *Arch. Neurol. & Psychiatry.* 1947, July, v. 58, No. 1, 14–23, 2 figs. [Refs. in footnotes.]

The author deals with his experiences in the Mediterranean war area, where malaria was a common disease among American armed forces, with special reference to the neuropsychiatric complications of malaria that were encountered. These complications simulated meningitis, encephalitis, cerebral tumour, vascular lesions and psychiatric disorders. Such "cerebral" forms of malaria were not exclusively caused by *P. falciparum* infections ; *P. vivax* was sometimes incriminated. The clinical history of an illustrative case is described.

A man aged 26 fell ill with a chill and slight fever. Two examinations of the blood were made but no parasites were found. Symptoms of meningo-encephalitis developed rapidly, with characteristic changes in the spinal fluid : the suspicion of a virus infection was not confirmed. Convulsions developed and the diagnosis of epilepsy was considered, but the presence of coma, a temperature of 102·20 F. and meningeal symptoms negatived this. Then followed an afebrile period of several days during which the cerebrospinal fluid became normal, but evidence of transient focal disturbances in the brain remained. Still no malaria parasites were to be found. On the 8th day a generalized convulsion occurred, followed by a Jacksonian fit on the right side : sodium amytal aborted a threatened "status epilepticus". Four days later a right homonymous hemianopia was detected, and persisted. On the 19th day of illness the temperature rose to 101·8° and *P. vivax* was found in the blood. Quinine was administered. All the symptoms cleared up quickly, except the hemianopsia. The case was undoubtedly one of malarial meningo-encephalitis with multiple neuropsychiatric manifestations. *Norman White*

ANDREWS, J. C. & CORNATZER, W. E. **The Metabolism of Cinchonine in Dogs and in Man.** *J. National Malaria Soc.* 1947, Dec., v. 6, No. 4, 246–50. [10 refs.]

The authors showed previously that cinchonine was absorbed more rapidly than quinine from the isolated intestinal loops of dogs. HIATT [this *Bulletin*,

1945, v. 42, 178] on the other hand, found that only low concentrations of the former were present in human plasma after oral administration compared with those of the other common cinchona alkaloids, indicating a possible difference in the rate of absorption of the two optical isomers cinchonine and cinchonidine. When the four alkaloids were given intravenously to man, HIATT & QUINN [this *Bulletin*, 1945, v. 42, 778] found that their distribution in the body was similar. It is possible therefore that the rate of metabolic breakdown varies in the case of these different alkaloids. Data were therefore obtained on the blood levels and urinary excretion of cinchonine in man and dog by means of the intestinal loop method of the authors [this *Bulletin*, 1945, v. 42, 534] in the animal experiments. The results indicated that cinchonine is metabolized more rapidly than cinchonidine or quinine in man. In the dog the rate of metabolic breakdown appeared to be much slower. The results are of interest, since some authors believe that the antimalarial effect of cinchona alkaloids is due to a metabolic product of those substances. *J. D. Fulton*

CHEN, G. **Influence of Pamaquine and Atabrine on the Enzymatic Degradation of Quinine.** *Proc. Soc. Exper. Biol. & Med.* 1947, Nov., v. 66, No. 2, 313–14, 3 figs.

KELSEY & OLDHAM [this *Bulletin*, 1944, v. 41, 260] found that, of various animal tissues, rabbit liver was richest in the enzyme, termed by them quinine oxidase, which converted the alkaloid to the substance which MEAD & KOEPFLI [*ibid.*, 1945, v. 42, 9] characterized as a 2-hydroxy derivative. A method has now been developed for the quantitative assay of this enzyme, and its inhibition by plasmoquine (pamaquin) and atebrin (mepacrine) have been investigated. For this purpose, fresh rabbit liver was homogenized in Ringer-Locke solution. On centrifuging, all the enzymic activity was found to be present in the supernatant fluid. The latter was therefore used in all the experiments, in which quinine in Ringer-Locke solution and the enzyme were incubated at 39°C. for appropriate times. Enzyme action was then inhibited by the addition of an equal volume of 4 per cent. caustic soda. The unchanged quinine was estimated by the fluorometric method of CHEN & GEILING [*ibid.*, 1945, v. 42, 348] in a Coleman photofluorometer, with the use of suitable filters when plasmoquine and atebrin were present. The relationship between the percentage degradation of quinine and the logarithm of liver concentration used was linear except in the early stages of the reaction and a roughly similar relationship held when the former values were plotted against the logarithm of reaction time. By choosing a reaction time of one hour, the graphs allowed the activity of an enzyme preparation to be determined. Both plasmoquine and atebrin inhibited the conversion of quinine. While the mode of action of these substances is not quite clear, it is believed that they act on the enzyme rather than on the substrate. *J. D. Fulton*

DEARBORN, E. H. **The Distribution of Quinacrine in Dogs and in Rabbits.** *J. Pharm. & Exper. Therap.* 1947, Oct., v. 91, No. 2, 174–7.

"The concentration of quinacrine in the plasma of rabbits and dogs shows marked variation. There is no significant correlation between the concentration of quinacrine in the plasma and that in the tissues of rabbits and dogs. The concentration of quinacrine in muscle and its ratio to the concentration in the plasma tend to increase in dogs on a constant daily dosage."

TRAGER, W. **The Rate of Asymptomatic Malarial Infection in White and Negro Service Troops taking Suppressive Atabrine.** *Amer. J. Hyg.* 1947, Nov., v. 46, No. 3, 336–40.

The author, in collaboration with BANG and others, has previously shown that malaria parasites may sometimes be found in thick blood films from men taking adequate suppressive doses of mepacrine and having no clinical symptoms of malaria [this *Bulletin*, 1947, v. 44, 503]. In Finchhafen, New Guinea, he made a study of three pairs of Army units, one unit of each pair consisting of whites, the other of negroes. The units of each pair were living under strictly comparable conditions as regards the risk of malaria infection. The men were all taking, or supposed to be taking, 0·1 gm. of mepacrine a day. The results of the study during the 4 to 6 weeks period of observation were as follows :—

	Unit					
	A	B	C	D	E	F
Race	White	Negro	White	Negro	White	Negro
Men studied	87	82	95	85	106	102
Average smears per man ...	5·3	5·5	3·8	3·8	3·7	3·8
No. with one positive smear ...	19	11	20	9	20	17
No. with two positive smears ...	3	2	3	1	2	1
Per cent. with parasites ...	25	15	24	12	22	17
No. from south-eastern U.S. ...	0	4	27	1	15	89
No. who had had clinical malaria in U.S.A.	0	0	2	0	3	19
No. who had had clinical malaria in New Guinea	0	0	1	1	0	1

Most of the parasites found were ring forms. A few old trophozoites were seen, but only one gametocyte (*P. vivax*). It is probable that all the parasites were *P. vivax*. Only one man had three positive smears (Unit E) ; he had parasite counts of 1, 32 and 55 parasites per 500 white cells in three successive weeks, but had no symptoms of malaria. Very few of the other positive smears contained more than 4 parasites per 500 white cells. The author has previously shown that the finding of these occasional parasites bears no relation to the mepacrine blood level. *Norman White*

PERK, D. **Mepacrine Psychosis.** *J. Mental Sci.* 1947, Oct., v. 93, No. 393, 756–71. [12 refs.]

Not all cases of psychosis in patients with malaria treated with mepacrine are necessarily true cases of mepacrine psychoses. It is possible that the symptoms began before the exhibition of mepacrine and were precipitated either by malaria or by circumstances antecedent to it, or the condition was present before mepacrine therapy and was aggravated by the drug. In true mepacrine psychoses, the symptoms are precipitated by the administration of mepacrine. Twenty-three cases of true mepacrine psychosis seen in the Middle East are described : all were males and British, except for two Palestinian Jews. The proportion of officers and N.C.O.'s to privates was as 11 to 12 and is said to be high compared with the ratio in the command [the ratio is not given]. The most common mental make-up of the patients was schizoid, 6 cases. The aetiology of mepacrine-precipitated cases is thought to be multifactorial and in addition to malaria, emotional stress may have contributed in 7 cases, recent battle stress in 3, and alcoholism in 2 cases. Eleven patients had had one or more attacks of malaria in the 18 months before the psychiatric episode. Three

patients gave histories of previous psychotic breakdowns and in one other psychotic symptoms appeared during a subsequent attack of malaria when quinine and pamaquin were given. Of the 23 patients, only one had been on suppressive mepacrine: he had taken 0·2 gm. for 9 months, and the breaking-off of his engagement is said to have precipitated the attack.

The psychotic symptoms appeared when the standard treatment for malaria was 3·4 gm. of mepacrine in 6 days. One-third of those affected developed mepacrine psychosis on the third or fourth day of treatment, the remainder usually within 7 days of the end of treatment. In one case, symptoms began in less than three days and in another (included as having been precipitated by mepacrine) not till 3 months after the cessation of mepacrine therapy [on the dose schedule given, it is very doubtful whether more than minimal traces of mepacrine would have been found in the body after this interval].

There was no significant difference in the time of recovery between those developing the psychosis early and those who developed it late.

The most frequent symptoms were schizophrenic and manic in type: malaria, on the other hand, more commonly produces a depressive reaction. The onset is almost invariably signalized by insomnia and in the non-depressive cases by a sudden change of behaviour, with noisy talkative excitement. The psychotic picture then develops rapidly: there is a brief phase for a day or two of features such as fleeting ideas of influence, loss of personality and reality sense and sometimes transient confusion and disorientation. This is followed by elation, euphoria and delusions of an exalted character. Eight typical case histories are recorded.

Fourteen of the 23 patients recovered within 6 months of the onset of symptoms, the quickest being in 14 days, the average 62 days: those with manic and schizophrenic symptoms recovered most quickly. Mepacrine psychoses occur more frequently in a slightly older age-group than do those due to malaria. Electrical convulsive treatment was used in six cases: 4 of these (two with schizophrenia and two with depression) improved but 2 remained unchanged: the number of convulsions ranged from 2 to 6, averaging 4·6.

Diagnosis requires differentiation from cerebral malaria and from an endogenous or biogenic psychosis.

It is stated that the medical attendant should be on his guard in exhibiting mepacrine to those who have had recent attacks of malaria, show evidence of hepatic derangements, have taken suppressive mepacrine in large doses or suffer from any factors which delay the excretion of mepacrine.

The danger signals which are said to call for the stoppage of mepacrine in the treatment of a malarial attack are staining of the skin and the occurrence of insomnia, alteration of conduct, restlessness, talkativeness and confusion.

[Few will agree with the contention that staining of the skin necessitates cessation of mepacrine therapy. Those in army commands serving in hyper-endemic malarial areas were almost all tinted yellow by mepacrine: eccentric some of them may have been, but they were not on the verge of a mepacrine psychosis.] *G. M. Findlay*

Buonomini, G. & Motta-Diana, A. Trattamento abbreviato con acridinici dell'attacco malarico sua utilità nella pratica dispensariale. [**Short Treatment with Acridine of the Malaria Attack and its Suitability for Dispensary Practice.**] *Settimana Med.* 1946, Aug. 3–31, Year 34, n.s., v. 2, Nos. 31/35, 64–8, 2 figs.

The "standard," treatment of malaria attacks in Italy with Italchina [an acridine derivative, see this *Bulletin*, 1941, v. 38, 34], has consisted hitherto

in the administration, to patients 14 years of age and upwards, of 0·3 gm. a day for five days in *P. vivax* infections, and for seven days in *P. falciparum* infections. The authors report the treatment of 211 cases of *P. vivax* malaria and 54 cases of *P. falciparum* malaria with larger doses for a period of 4 days only in both types of infection, the doses being 0·5–0·6 gm. a day for adults. The results are compared with those obtained by the treatment of 1,613 cases by the "standard" method. The observations were made in an endemic area of Sicily. The blood of all patients was free from parasites on the 4th day; in 98 per cent. of the *P. vivax* infections on the 3rd day. There was no significant difference in the incidence of relapses after the two methods of treatment. Symptoms of intolerance to the drug were absent or insignificant in the vast majority of cases. One patient developed transient psychotic symptoms.

The short system of treatment possesses obvious advantages for dispensary practice, in rural areas especially, and is recommended. *Norman White*

PINTO, G. de S. Sobre a ação da paludrina nos acessos de malária. [**The Action of Paludrine in the Treatment of Malarial Attacks.**] Reprinted from *Folha Med.* 1947, Aug. 25, 12 pp.

A severe outbreak of malaria in the early months of the year occurred in Itapema, a district in the Guaruja *municipio* in the Isle of Santo Amaro near Santos, Brazil. The outbreak was attributed to the influx of very large numbers of chronic malaria sufferers. (The vector *A. tarsimaculatus* was surprisingly difficult to find, only exceptionally being captured in houses.) About 90 per cent. of the infections were caused by *P. vivax*.

Paludrine was used in the treatment of 1,068 patients with acute malaria. Of 557 patients treated with a single dose of 2 tablets, 0·20 gm., febrile symptoms were promptly suppressed in 89·4 per cent. When 4 tablets were given, in two doses, the success rate was 97·7 per cent. (96 cases).

Norman White

KIERLAND, R. R. & MCCREIGHT, W. G. **The Termination of Therapeutic Malaria with Chloroquine.** *Amer. J. Syph.* 1948, Jan., v. 32, No. 1, 57–8.

The authors refer to previous work on the use of chloroquine in the treatment of malaria, and especially in acute relapsing *P. vivax* infections [this *Bulletin*, 1948, v. 45, 37].

They have used chloroquine to terminate therapeutic malaria in 25 patients suffering from central nervous syphilis, who had been inoculated therapeutically with a strain of *P. vivax* which had been in use for more than 20 years. The inoculation took the form of an intravenous injection of 5 cc. of *vivax*-infected whole blood direct from patient to patient. The incubation period varied from 1 to 12 days and each patient had between 7 and 10 paroxysms before termination was attempted: the results obtained with chloroquine could not be shown to be affected by the incubation period or by the number of paroxysms.

Each patient was given 1 gm. of chloroquine, followed in six hours by 0·5 gm. and then 0·5 gm. again in twenty-four and forty-eight hours (total 2·5 gm.). In two cases, a total of 3 gm. was given. The chance of vomiting was reduced when the drug was given after the patient's temperature had fallen below 103°F., and this also reduced the likelihood of an additional paroxysm. In 21 cases, no febrile episodes occurred after the treatment had started, but in 4 an additional paroxysm occurred within twenty-four hours: in all these 4 cases, the drug had been given when the temperature was rising.

Only one patient reported a side-reaction, namely a mild and transient gastro-intestinal upset : no skin reactions were reported.

In 14 cases in which the blood was examined for parasites after chloroquine had been given, parasites were found to have disappeared within 24 hours of the initial dose in 2, within 48 hours in 4 and within 72 hours in 7. In one case, the parasites persisted until the 5th day. One case was negative microscopically throughout. No relapses have been noted during follow-up periods of 2 to 8 months after treatment. *H. J. O'D. Burke-Gaffney*

CURD, F. H. S., GRAHAM, W., RICHARDSON, D. N. & ROSE, F. L. **Synthetic Antimalarials. Part XXII. Some Quinolylamino-substituted Pyrimidine Derivatives.** *J. Chem. Soc.* 1947, Dec., 1613–19.

DOUGLAS, B., JACOMB, R. G. & KERMACK, W. O. **Attempts to find New Antimalarials. Part XXVI. Further Derivatives of *p*-Phenanthroline.** *J. Chem. Soc.* 1947, Dec., 1659–61.

COVELL, G. **A Brief Review of the History and Development of the more Important Antimalarial Drugs.** *Indian J. Malariology.* 1947, June, v. 1, No. 2, 231–41. [13 refs.]

WALTON, G. A. **On the Control of Malaria in Freetown, Sierra Leone. I. *Plasmodium falciparum* and *Anopheles gambiae* in relation to Malaria occurring in Infants.** *Ann. Trop. Med. & Parasit.* 1947, Dec., v. 41, Nos. 3/4, 380–407, 7 figs. [56 refs.]

The author was the first medical entomologist appointed to the Government of Sierra Leone. At that time, 1943, malaria control, on a large and comprehensive scale, was begun as an urgent wartime necessity. By co-operation with the three Services, mosquito breeding in the western and eastern rural areas and Central Freetown was controlled by larvicides. An extensive network of mosquito catching stations indicated the anopheline house population from week to week. This paper is an assessment of the effect of these measures during the period June 1944–June 1946, on malaria incidence in Freetown.

Freetown has some 8,000 houses and population of 80,000, and is situated along a coastal plain less than a mile wide and backed by heavily wooded mountains. Humidity is high all the year and there is a heavy rainfall of about 130 inches per annum ; five months are almost dry, but July and August have 35 inches each. That the house population of *Anopheles gambiae* was very markedly reduced is shown by the following table :—

Number of female A. gambiae *per 1,000 rooms per month in Freetown, June, 1944 to May, 1946*

June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Apr.	May
261	447	189	55	8	4	7	11	10	4	7	64
330	116	37	18	4	1	15	23	20	27	20	147

The anopheline infective density is a means of expressing the malaria-transmitting ability of an anopheline population. The number of infected *A. gambiae* for each average Freetown room from October 1944 to March 1946, is calculated at 0·07 ; in other words, there was on the average only one infected *A. gambiae* in every 14th room per 18 months. Applying this conclusion to the human population of Freetown for that period, one in 56 persons would receive an infected mosquito bite ; this figure is a maximal estimation.

Malaria in African Infants

Parasite Infestation of Infants.—Data of infestation placed in age-groups of 3 months and plotted semi-logarithmically, is as follows :—

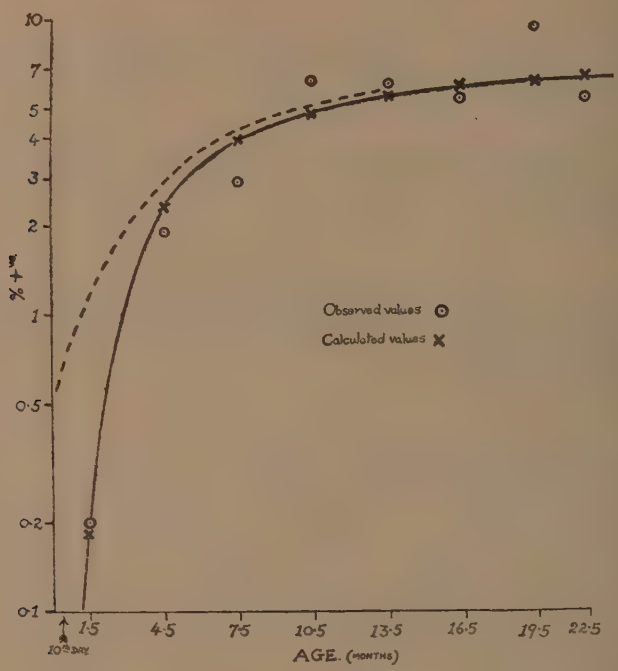


Fig. 1.—Graph showing the rate of increase with age in percentage malaria infestation of infants. The black curve is based on the recognition of not less than four trophozoites ; the dotted curve includes all positive findings, but the true curve of infestation is probably even higher, since some infections must have been missed. [Fig. 7 in original.]

Effect of Mosquito Control.—The comparable numbers of infected bites per room per year in an eastern rural suburb (Kissy) in 1931, and in Freetown in 1931 and 1945, were roughly 250, 30 and 0·07.

Parasite infestation in age groups in the same areas for the years 1931 and 1945 is illustrated as follows :—

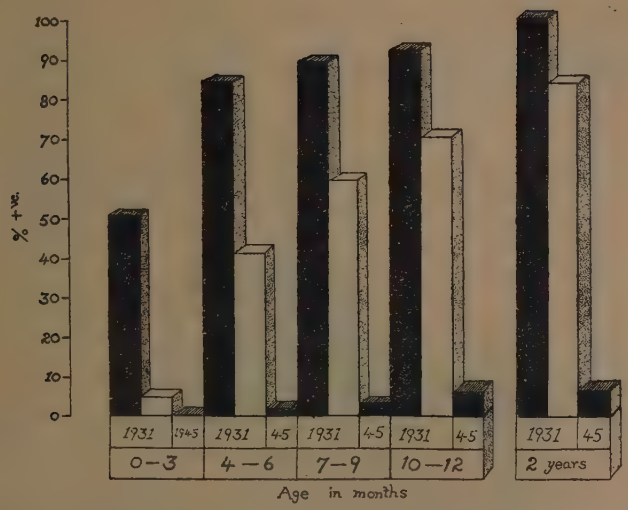


Fig. 2.—The effect of mosquito control on the parasite-index of infants at different ages. The tall black columns show the parasite-indices of infants living in the rural village of Kissy, close to Freetown, in 1931 ; the white columns show the parasite-index of Freetown infants in 1931, and the short black columns show the same for the period 1944–46. [Fig. 5 in original.]

[That this marked reduction occurred only in Freetown, and not also in the surrounding country, is shown by the work of Davidson in 1946 ; his summarized results for parasite indices in children were 80 per cent. for coastal and 73 per cent. for interior villages.]

Relation between the Anopheline Infection-Rate and the Malaria Parasite-Rate in Infants

A statistical method is described for estimating the number of infective mosquito bites and the associated parasite-indices ; the calculated result is summarized in Table VI below.

Rate of Infection of Infants.—It was possible to keep track of 50 infants for eighteen months or more ; 12 to 15 infections were received, that is 1 in 4. The considerable discrepancy between this figure and the above-mentioned 1 in 56 persons is believed to be due to infections acquired outside the controlled area.

Duration of Infection in Infants.—A table summarizes monthly blood examinations of 31 infants up to the 24th month. The difficulty of following-up cases has caused many omissions, but the data do throw some light on the duration of single infections ; the average appears to be about 9 months.

Gametocyte Production.—It was observed that gametocytes appeared for one month only, during which trophozoites were suppressed. The mean number of trophozoites unaccompanied by gametocytes was 1,000 per 150 fields, while the mean number with gametocytes was 14.

TABLE VI

Parasite-indices produced in a group of young children by various numbers of infective mosquito-bites received in a year

No. of infective bites per child per year	Calculated parasite-rate per cent. in young children
0·01	0·26
0·10	2·57
0·20	5·07
0·30	7·50
0·40	9·90
0·50	12·20
0·70	16·60
1·00	22·90
1·50	32·30
2·00	40·50
3·00	54·20
4·00	64·70
5·00	72·70
7·00	83·80
10·00	92·60
20·00	99·45
30·00	99·96
50·00	99·99

Severity of Infections in Infants.—From the date available it would appear that, contrary to what would be expected, the intensity of infection, as measured by the number of trophozoites in the blood, increases with age, at least up to the age of 15 months. Apparently the infants become increasingly susceptible as they grow older. The figure below attempts to portray the change in parasite quantity with age.

Previous Work on African Infants.—A summary is given of previous work ; in the light of this and his own experience the author concludes that, for some reason, very young infants are not bitten by anophelines to the same extent as older children, or that, when bitten by infective mosquitoes, they possess some mechanism which prevents the appearance of plasmodia in the peripheral blood.

Whatever brings about active proliferation of the reticulo-endothelial system of the mother might well do the same to the unborn child and hence the newly-born infant would be ready to deal with its first infection.

[The author has made a most valuable contribution to knowledge of malaria transmission in addition to proving the efficiency of larvicidal methods of control when backed by a sound organization ; he claims a " virtually 100 per cent. effective " result. The mass of information, with a full list of references, requires to be digested in the original by readers interested in the subject.]

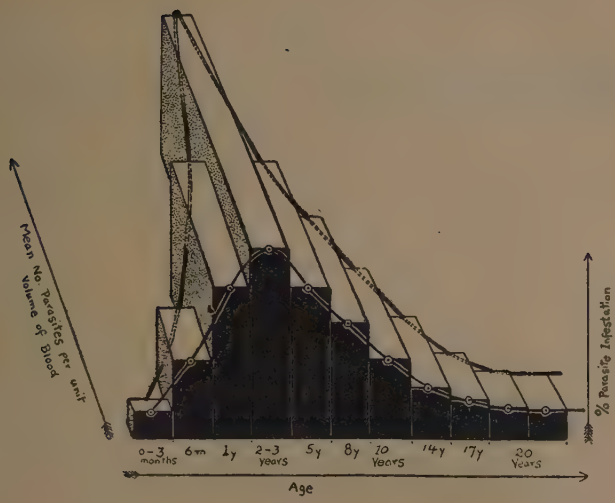


Fig. 3.—Three-dimensional hypothetical representation of the variation of intensity of parasite infestation at different ages.

The horizontal axis shows age, increasing from left to right; the older age-groups are foreshortened. Based on the age-group scale the histogrammatic representation in the vertical axis depicts the change in percentage parasite infestation with age. Superimposed on this is the graphic representation of the same data. The depth of the receding columns represents the mean number of parasites per unit volume of blood (intensity) in each age-group, the scale being on a horizontal axis, at right angles to the axis depicting increasing age. The differences in the intensities of parasite infestation at different ages are greatly reduced; nevertheless the great variation in the degree of parasitization at different ages is quite clearly shown. The receding curve passing through the distal margins of the columns represents the change in parasite 'quantity' with age. [Fig. 6 in original.]

[Figures reproduced from the *Annals of Tropical Medicine and Parasitology*.]

R. Ford Tredre

THOMSON, R. C. Muirhead. **The Effects of House Spraying with Pyrethrum and with DDT on *Anopheles gambiae* and *A. melas* in West Africa.** *Bull. Entom. Res.* 1947, Dec., v. 38, Pt. 3, 449–64. [23 refs.]

A. gambiae and *A. melas* are well known house-frequenters by day, but the author submits evidence of out-door resting places and is of opinion that the number of mosquitoes caught by routine methods in houses by day may be only a small proportion of the mosquitoes actually feeding there at night. Ninety per cent. of feeding by *A. melas* and *A. gambiae* takes place between midnight and dawn, and it is possible for the mosquito to spend only an hour or two of the 48-hour gonotrophic cycle in the house.

Three villages near Lagos were mass-sprayed with "Pyefly" diluted 1 in 59 with kerosene, at the rate of $\frac{1}{2}$ to $\frac{3}{4}$ ounce per 1,000 cu. ft., with the results shown above. In the selection of these villages, care was taken to ensure that there was no infiltration of infected mosquitoes from other areas. Even the intensive spraying of the last period failed to bring about a substantial reduction

Spray-killing in Houses with Pyrethrum in Kerosene

TABLE I

Mass spraying of village houses with pyrethrum in kerosene. Incidence and infectivity of melas *and* gambiae. *December 1945–April 1946*

Treatment	Number and period of collections	*Gambiae* and *melas* per 10 bedrooms	Mosquitoes dissected	Glands positive	Sporozoite rate
	8				
Preliminary survey. Houses untreated	18/xii to 19/i				Per cent.
	15	33	485	17	3·5
All houses sprayed four times weekly from 19/i	1/ii to 7/iii				
	7	11	400	12	3·0
All houses sprayed six times weekly from 7/iii	14/iii to 2/iv				
		12	247	18	7·3

in the numbers of mosquitoes in houses, though the increase in the sporozoite rate may be due partly to the increase in breeding of *A. gambiae* expected at this time of the year.

As a result of the use of experimental huts provided with suitably designed window traps in an area infested with *A. melas*, evidence is offered to explain the results of village spraying. In short, in an untreated hut of the local type the number of blood-fed female mosquitoes found resting by day represent $\frac{2}{3}$ to $\frac{3}{4}$ of the total numbers feeding there the previous night; but in the hut sprayed daily with pyrethrum in kerosene the numbers found in the hut by day represent only $\frac{1}{5}$ of the total feeding there at night. Pyrethrum in kerosene has an irritant effect on many blood-fed *A. melas*, driving them out of the house after feeding; it also has a repellent effect, but it discourages entrance to the house only if an alternative untreated house is available; female *A. melas* are not attracted to animals, nor are they driven to animal feeding by mass spraying of human habitations; they prefer to enter the latter at night, to feed and leave almost at once. As a corollary to these conclusions, the author observes that however efficient spray-killing may be in estimating the total house- or room-catch, it should not be used in the same house more than once a week, otherwise the results may be affected by a shift of mosquitoes from inside the house to outside resting-places.

The author concludes:—

"The fall in the number of mosquitoes resting by day in houses after spraying is now seen to be caused, not by any great reduction in the population as a whole, but rather to a shift from indoor to outside resting places. The number of mosquitoes killed by even the most intensive spraying represents such a small proportion of the whole that the average length of life may be little affected, the sporozoite rate remaining at much the same level as before."

DDT in Kerosene as a Residual Insecticide

In the light of the observations on pyrethrum, the author proceeded to the investigation (by similar methods) of the effects of DDT in kerosene as a residual insecticide. The mass treatment of village houses by the usual methods produced the expected result, namely that house catches fell practically to zero and remained low for the nine weeks of observation.

Behaviour of A. melas *in Experimental Huts*

TABLE V

Treatment of experimental huts with DDT. One hut treated at rate of 100 mgm. DDT per sq. ft. Other hut untreated. Catches refer to freshly blood-fed Anopheles (*95 per cent.* melas, *5 per cent.* gambiae). *Window traps record mosquitoes leaving hut after feeding*

		Before treat-ment	After spraying					
			1 Week	2 Week	3 Week	4 Week	5 Week	6 Week
Number of visits		8	5	5	6	6	3	4
Treated hut	Hut catch ...	77	0	0	1	0	1	0
	Window trap	27	44	89	176	255	133	178
Untreated hut	Hut catch ...	91	189	244	390	140	138	194
	Window trap ...	25	56	12	223	294	123	35

TABLE VI

As in Table V, but experimental hut treated at rate of 250 mg. DDT per sq. ft.

		Before treat-ment	After spraying			
			1 Week	2 Week	3 Week	4 Week
Number of visits		5	4	6	5	3
Treated hut	Hut catch ...	189	0	0	0	0
	Window trap ...	56	2	28	157	82
Untreated hut	Hut catch ...	273	196	390	115	138
	Window trap ...	40	10	223	245	123

No dead *Anopheles* were found on the floor-matting of the treated hut; the mortality, during 48 hours after feeding, among mosquitoes leaving the hut was practically nil. By a separate experiment, it was shown that the absence of mosquitoes from the hut for ten days after treatment is more likely to be due to the repellent effect of a heavy dosage of kerosene than to the presence of DDT.

In the case of an isolated village, outside resting-places had been found and kept under observation for many months; 113 *A. melas* caught in these outside resting-places had a sporozoite rate of 2·7 per cent. During a period of five weeks after treatment of the village with DDT in kerosene (200 mgm. DDT per sq. ft.), 295 blood-fed and gravid mosquitoes were caught in the outside resting-places, with a sporozoite rate of 2 per cent.; infected mosquitoes were still found at the 5th week.

Conclusion.

The sharp fall in house catches after treatment with DDT in kerosene does not necessarily mean a corresponding reduction in mosquito population or biting activity. The most obvious effect of the treatment is to bring about a

complete shift from indoor to outside resting-places. Furthermore, the sporozoite rate of those mosquitoes caught outside is such as to suggest that malaria transmission is still possible.

[This work rightly draws attention to the fallacies associated with the indiscriminate use of DDT in kerosene applied as a residual insecticide in West Africa. Health officers there might well infer that the residual insecticide method is valueless as a measure of malaria control. On the contrary, the author's valuable paper should stimulate further investigation.

Using Gammexane in kerosene in Sierra Leone, DAVIDSON (this *Bulletin*, 1948, v. 45, 157) produced evidence to show that the treatment of houses in part of an area reduces the mosquito population, not only in that part, but also in adjacent parts one to two miles distant; the area concerned was a coastal strip six miles long with a string of seven villages, of which the first, third and sixth were untreated. Similar results were obtained in a group of inland villages.] *R. Ford Tredre*

PENIDO, H. M., AZEVEDO, N., PINTO, D. B., BEZERRA, F., Jr., DE SOUSA, E. F. & MOURA, F. P. Malária no vale do rio Doce. Organização e execução de serviços antilarvários. [**Malaria in the Valley of the River Doce: Organization and Activities of the Antilarval Services.**] *Rev. Hig. e Saúde Pública.* 1947, July–Sept., v. 5, No. 2, 3–25, 2 maps.

This paper describes in detail the antilarval work carried out in the valley of the River Doce, in the State of Minas Gerais, from August 1943 to June 1947 [see above]. Here *A. darlingi* is the sole vector. Chief reliance was placed on Paris green. The marked decline in malaria prevalence in certain places indicates the success achieved. *Norman White*

BRAGA, E., PENIDO, H. M., BASSÈRES, M. S., PINTO, D. B., BEZERRA, F. P., Jr. & MOURA, F. P. Malária no vale do rio Doce. Expurgo domiciliar com DDT em suspensão aquosa. 1ª fase. [**Malaria in the Valley of the River Doce: Treatment of Habitations with Aqueous Suspension of DDT.**] *Rev. Hig. e Saúde Pública.* 1947, July–Sept., v. 5, No. 2, 26–59, 3 maps & 3 charts. [14 refs.]

In September 1946, the DDT spraying of houses was commenced as an antimalaria measure along 120 kilometres of the Vitória-Minas Railway in the most malarious parts of the valleys of the Rivers Doce and Piracicaba in the State of Minas Gerais [see above]. The width of the area treated varied from 3 to 15 kilometres. The total area was about 1,500 square kilometres, containing a population of about 20,000 in 5,000 houses. An aqueous suspension of DDT was applied (5 per cent.), at the rate of 2 gm. per square metre. In January 1947, a second application was begun. About 85 per cent. of all houses were treated. The almost complete absence of *A. darlingi* from houses treated, a marked fall in the number of malaria parasite carriers and a very notable fall in the number of persons applying for treatment for malaria, testify to the noteworthy success achieved. Very full details are given of the work carried out. *Norman White*

GRAMICCIA, G. & SACCÀ, G. Note sulla infezione da *P. gallinaceum* nel pulcino. Considerazioni sul significato biologico del ciclo endoistiocitario dopo inoculazione di sangue. [**Biological Significance of Exoerythrocytic Cycle of *P. gallinaceum* in Young Chicks.**] *Riv. di Parassit.* Rome. 1947, Dec., v. 8, No. 4, 213–19. English summary.

The inoculation of young chicks 5–8 days old with blood infected with *P. gallinaceum* produces a more severe infection than when adult chickens are

inoculated. The young chicks first show exoerythrocytic forms on the 11th day of the blood infection, which is always fatal. The author interprets this period of eleven days as a cycle wherein the parasite attempts to repeat those phases that were omitted because of the method of inoculation. In the case of *P. elongatum*, blood inoculation is followed at the same time by both erythrocytic and exoerythrocytic development, while in the case of gametocytes these appear after a number of erythrocytic cycles. *C. M. Wenyon*

TONKIN, I. M. & HAWKING, F. **Growth of Protozoa in Tissue Culture. IV.** *Plasmodium lophurae*, **Exoerythrocytic Forms,** *in vivo* **and** *in vitro*. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Dec., v. 41, No. 3, 407–14, 23 figs. (16 on 3 pls.).

By means of sporozoites obtained from *Aêdes albopictus* infected by feeding on chickens harbouring *Plasmodium lophurae*, infection was produced in young turkeys. The observations of PORTER and LAIRD were confirmed that infection of the turkeys was associated with the production of exoerythrocytic schizonts which resembled those of *P. gallinaceum*. With spleen material removed from one bird tissue cultures were made. These resulted in the development of exoerythrocytic schizonts which again resembled those obtained by tissue culture of *P. gallinaceum*. The exoerythrocytic schizonts showed both macro- and micro-merozoite formation. The various stages in sections of tissues of the young turkeys and in the tissue cultures are illustrated in a series of black and white drawings and many other forms are shown in photo-micrographs. *C. M. Wenyon*

RIGDON, R. H. & MCCAIN, B. E. **Some Factors that influence the Degree of Parasitemia in Ducks infected with** *P. lophurae*. *Amer. J. Trop. Med.* 1947, Nov., v. 27, No. 6, 673–81, 7 figs. [19 refs.]

Young ducks 2–4 weeks old, when given a lethal dose of *P. lophurae* die at the height of the parasitaemia or when the parasites are decreasing in number. Some ducks, however, survive the infection, which may reach a figure of 400 infected cells per 500 red blood corpuscles on the 5th day of infection. In the survivors, the number of parasites rapidly decreases, so that in 48 hours only 5–10 parasitized cells per 500 red blood corpuscles are present. These ducks rapidly return to normal and within 5–7 days show no abnormalities in their haemogram. It seems improbable that the cells of the reticulo-endothelial system which are filled with pigment at the crisis are able to remove from the circulation the large number of parasites then present.

It has been shown that ducks with polycythaemia have larger numbers of parasites than normal ducks, while transfusion of infected ducks with normal red blood cells will prevent the decrease in the parasites which follows the peak of the infection. Another factor which will increase the number of parasites is oxygen; for ducks placed in a chamber with a concentration of oxygen of 30–80 per cent. show a greater number of parasites in the peripheral blood. Again *P. lophurae* prefers mature red blood cells to those that are young and there is a marked diminution of adult cells when the parasitaemia is high. These young cells are poor in haemoglobin and the oxygen-carrying ability of the blood decreases during the infection.

It has recently been shown that if blood for inoculation is treated with CO_2 by bubbling the gas through it, many of the parasites are so altered that it fails to produce the same degree of parasitaemia as when oxygen or nitrogen are bubbled through it. Observations have shown that malaria-infected ducks develop a severe acidosis which is directly related to the anaemia. The

CO_2 content of the plasma, however, remains approximately normal until the anaemia falls to below one million, after which it declines steadily till the time of death. After the administration of ammonium nitrate to ducks, there occurs a severe acidosis with no anaemia, while there is a decrease in the CO_2 content of the plasma. Administration of sodium bicarbonate is followed by a severe alkalosis with only slight anaemia and increase in the degree of retention of CO_2. It is concluded that the acidosis which occurs in malaria may not result entirely from the anaemia, since ducks with an acidosis following ammonium nitrate administration have no anaemia. To determine the relation of the total number of red cells to the CO_2 in the plasma, the CO_2 content was divided by the number of red cells in millions. This factor was plotted against the total number of red cells. A similar factor was obtained from ducks which had received ammonium nitrate and sodium bicarbonate. The points in the chart for the ducks with malaria parallel those of the ducks which had sodium bicarbonate. When the figure given by dividing the CO_2 content of the plasma is plotted against the number of parasitized red cells, it is found that the CO_2 content increases with the number of parasitized red cells. The greatest increase occurs when the parasitized cells number 250 or more per 500 red cells. It is thought that the CO_2 content may be sufficient to injure or kill some of the parasites. *C. M. Wenyon*

TRYPANOSOMIASIS

HARDING, R. D. & HUTCHINSON, M. P. **Sleeping Sickness of an Unusual Type in Sierra Leone and its Attempted Control.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 481–512, 1 map.

In 1939 and 1940 medical surveys showed that sleeping sickness existed in an area of about 200 square miles on the eastern boundary of Sierra Leone adjoining French Guinea, where the disease had been treated since 1934. Mass campaigns were decided on and were carried out in 1941, 1942 and 1944.

Sleeping sickness in Sierra Leone is caused by *Trypanosoma gambiense* and is spread by the bite of the tsetse fly *Glossina palpalis*. In the campaigns diagnosis was made by microscopical examination of the fluid obtained by puncture of enlarged superficial lymphatic glands and of blood films, but, as trypanosomes were found in the glands four times as often as in the blood, the latter was only examined when gland puncture gave negative results or when the glands were not palpable.

In 1941 the disease was clinically like that in other parts of Sierra Leone but in 1942, in the central part around the town of Fuero, some differences were observed : trypanosomes were found in the blood as often as in the glands and were unusually numerous in the blood of some persons ; many patients had no enlarged cervical glands and showed no symptoms even when the blood contained many trypanosomes. All the inhabitants were examined and all cases of sleeping sickness were treated, but no further work was possible for over a year. A survey in 1944 showed that the unusual form of the disease (" Fuero type ") had spread considerably and the infection rate was nearly doubled ; in Fuero itself, trypanosomes were found in the blood ten times as often as in the glands but in 1945 this disparity was less.

Seventy-five patients were left untreated and examined weekly for 2 months and 17 others, also untreated, were examined monthly for 7–9 months : nearly all showed no symptoms or physical impairment. Trypanosomes appeared in the blood irregularly and it was reckoned that about 35 per cent. of cases would escape diagnosis at any single examination ; even patients with an increased

cell-count in the cerebrospinal fluid often had no symptoms. There seemed to be a state of equilibrium between host and parasite and some spontaneous recoveries probably occurred, but observation for several years would be required to confirm this. Although from a quarter to a third of the population of Fuero had been infected, the population had not decreased.

In experimentally infected monkeys the disease was also mild; in infected guineapigs the trypanosomes were resistant to intraperitoneal injections of human blood serum and sensitive to tryparsamide—characters of *T. gambiense*. [Injection of human serum into guineapigs infected with *T. rhodesiense* will, in certain doses, banish the trypanosomes for several days.]

Prophylaxis.—The population (15,550) of the whole area received prophylactic injections of antrypol (germanin) or pentamidine isethionate and special observations were made of the 2,500 inhabitants of the central part, including Fuero; all the latter were examined by gland puncture and blood films and lumbar puncture was done in nearly all infected persons. Some of the sleeping sickness cases were fully treated, others left untreated, and still others received prophylactic doses of antrypol or pentamidine to see whether this would suppress the infection. A prophylactic injection was given to 1,765 uninfected persons and 542 were left as controls. The results with various prophylactic doses are shown in tables.

In infected persons given prophylactic doses, the blood showed no trypanosomes for at least 7 months, therefore missed cases of infection receiving a prophylactic dose would hardly infect tsetse flies during that period but their recognition later would be difficult and they might eventually become infective. No gland infections and only 2 blood infections were found after 7 months among 1,498 uninfected persons examined who had received prophylactic injections—a rate of 0·1 per cent.—while among 471 controls there were 12 gland infections and 12 blood infections (5·1 per cent.).

In two other areas of Sierra Leone, where sleeping sickness of the usual type was present, prophylactic injections proved very effective; after 1–2 grammes of antrypol, only 2 cases occurred among 772 people (0·26 per cent.) and after 100–300 milligrammes of pentamidine no infection was found among 921 people while among 2,407 controls 22 cases (0·92 per cent.) occurred. The period of observations in these investigations was 10 months.

The authors discuss the results and conclude that prophylaxis by drugs is more effective than treatment of cases in checking an epidemic and acts more quickly. Pentamidine is preferable to antrypol, being at least as efficient and having fewer undesirable side-effects; a single intramuscular dose of 150 milligrammes is the best for a mass campaign. The importance of the possible masking of symptoms by prophylactic injections remains undecided.

J. F. Corson

GELFAND, M. **Transitory Neurological Signs in Sleeping Sickness.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Oct., v. 41, No. 2, 255–8.

The author (writing from Salisbury, S. Rhodesia) discusses the usual symptoms and signs which indicate involvement of the nervous system in sleeping sickness, remarking that these are changes in personality rather than true neurological signs. This is to be expected in view of the fact that the disease is essentially a form of encephalitis, pathologically not unlike general paralysis of the insane. If paralyses do occur, they are usually not extensive, and the author has been unable to trace any record of transient paralyses in sleeping sickness. He now describes a case in an adult African, in which symptoms pointed to a form of encephalitis or tuberculous meningitis, with swelling of the right optic disc, a right extensor plantar response, and, shortly afterwards, a

right facial palsy which disappeared spontaneously in about 2 weeks. At this time no definite evidence of trypanosomiasis could be obtained, but about 6 weeks later the gradually worsening symptoms led to another examination of the spinal fluid, in which trypanosomes were now abundantly found. The type of disease was not definitely determined, but was probably Rhodesian. Treatment with tryparsamide and pentamidine was successful, but the patient left hospital when the course was completed, and his later history is not known.

Charles Wilcocks

VAN HOOF, L., HENRARD, C. & PEEL, E. Notes sur l'action curative et préventive de la propamidine. [**The Therapeutic and Prophylactic Action of Propamidine.**] *Ann. Soc. Belge de Méd. Trop.* 1947, June 30, v. 27, No. 2, 257–63.

The authors describe their experiences in the treatment of different types of sleeping sickness cases in Léopoldville. Propamidine (isethionate) was used in daily doses of 1 to 2 mgm. per kilo intramuscularly till a total of 25 mgm. per kilo was given: in 5 hospitalized patients thus treated in 1943, no relapse occurred. In one arsenic-resistant case with a moderate increase in leucocytes in the cerebrospinal fluid a return to normal had not taken place at the time of writing, and one non-arsenic-resistant case did relapse. Further cases responded less well to treatment and trypanosomes disappeared but slowly from the peripheral blood. Immediate toxic effects from the drug were of minor importance, but paralysis occurred later in some cases. Nervous symptoms appeared to be avoidable if the drug were given intramuscularly. The authors confirm the abortive action of the drug described below by EERAERTS. Prophylactic experiments on guineapigs with a single dose of propamidine gave similar results to those previously obtained by the authors with pentamidine [this *Bulletin*, 1944, v. 41, 928]. In human cases, the protection afforded by 5 mgm. per kilo was estimated to last 6 months, as with pentamidine. The two drugs thus appear to have comparable protective and curative properties against *T. gambiense* infections, but propamidine seems to be more toxic, giving rise to paresis and paralysis.

J. D. Fulton

EERAERTS, W. La propamidine comme préventif dans deux foyers de trypanosomiase humaine au Congo Belge. [**Propamidine as a Preventive in Two Foci of Human Sleeping Sickness in the Belgian Congo.**] *Ann. Soc. Belge de Méd Trop.* 1947, June 30, v. 27, No. 2, 201–24. [20 refs.]

The author refers to the earlier work of VAN HOOF *et al.* [this *Bulletin*, 1944, v. 41, 928; 1946, v. 43, 536] on the value of pentamidine in prevention and treatment of Gambian sleeping sickness in the Belgian Congo. He himself has carried out comparable field trials with propamidine, in two active foci of infection in the Kwango district of Léopoldville province. Two injections of the drug in 4 per cent. solution were given deeply into the muscles, with an interval of six months between doses. For adults the maximal dose was 5 mgm. per kilo [presumably of isethionate] with gradations according to age. In all, about 8,000 Africans were injected, none of whom was clinically ill. At the time of the first injection, the disease was spreading rapidly in one district. Examinations were made at intervals of 2 or 4 months after the injections and again at the end of six months, when no infection could be found in those who had received the drug. Four and nine months after the second injection the same state of affairs held. In a second focus of infection the trypanosomes were arsenic-resistant and the disease was spreading rapidly with 28·5 per cent. of new cases in a total of 41·1 per cent. of the population infected. Three and six

months after injection with propamidine, no fresh cases were present among those treated. From his experiments the author concluded that protection lasted from 6 to 8 months.

The drug does not clear the peripheral blood rapidly and he considers its chief rôle to be that of a preventive rather than curative agent. There were some minor toxic symptoms from the drug, including epigastric pain, transient albuminuria and mild paresis of limbs. Two aged patients exhibited more serious signs of intoxication, including lowered blood-pressure, tachycardia, dyspnoea, severe epigastric pain and coma, but recovery was complete after 12 hours. The abortive action of propamidine has not previously been recorded since smaller doses of the drug have generally been used. The large dose of 5 mgm. of propamidine per kilo, however, brought about this result in a large percentage of pregnant women. Half this dose was well tolerated.

The mechanism of the protection afforded by propamidine is not yet clear, but the practical achievement of wiping out one focus of infection and nearly eradicating another is of the utmost importance. The results compared favourably with those obtained by the use of Bayer 205, and advantages claimed for propamidine over Bayer 205 are its greater solubility and lesser toxicity, as well as the fact that it can be given intramuscularly.

J. D. Fulton

WILLIAMSON, J. & LOURIE, E. M. **"Melarsen" and "Melarsen Oxide".** *Nature.* 1948, Jan. 17, 103–4. [14 refs.]

VAN HOOF [this *Bulletin*, 1947, v. 44, 1048] found that melarsen oxide, a new type of phenylarsenoxide containing a melamine group, was active against arsenic-resistant trypanosomes in the field. His findings have been confirmed by the present authors in the laboratory. They point out that arsenic resistance in the case of trypanosomes in fact involves resistance to the substituted phenyl group to which the arsenic is attached. It was recognized in the earliest investigations that trypanosomes made resistant to atoxyl failed to exhibit this property on treatment with aromatic arsenicals containing acidic groups. KING & STRANGEWAYS [this *Bulletin*, 1943, v. 40, 20] suggested three ways in which the different types of aromatic arsenoxides may be distributed in or on the trypanosome, while the final reaction in which the parasite was killed probably involved in all cases combination between the arsenoxide and sulphydryl groups in the trypanosomes. Interference experiments were used to provide evidence that melarsen oxide may combine with the trypanosome in still another way. Thus melamine itself and Surfen C, which also contains a melamine group, were found to interfere with the therapeutic action of melarsen oxide on a normal strain of *T. rhodesiense* as did *p*-aminobenzoic acid with that of γ-(*p*-arsenosophenyl) butyric acid and glutathione with arsenoxides in general. The authors conclude that the mode of combination between trypanosomes and melarsen oxide is different from that of other arsenoxides, although the final lethal effect of the latter is produced in the same way. The interference between melarsen oxide and Surfen C appears to depend on the common possession of a melamine group.

J. D. Fulton

VANDERPLANK, F. L. **Seasonal and Annual Variation in the Incidence of Trypanosomiasis in Game.** *Ann. Trop. Med. & Parasit.* 1947, Dec., v. 41, Nos. 3/4, 365–74. [15 refs.]

These investigations were made in Tanganyika Territory from June 1939 to June 1944; 378 wild mammals belonging to 38 species were shot and their blood examined microscopically for the presence of trypanosomes. The results

in 135 of them [153 in the text] were recorded in a previous paper (*Trans. Roy. Soc. Trop. Med. & Hyg.*, 1942, v. 35, 319). Similar observations by E. F. THOMSON in Northern Rhodesia are also shown in a table.

Giraffes showed the highest rate of infection (37 per cent.), then roan, eland, zebra, impala and wart-hog in that order while no trypanosomes were found in carnivores, monkeys and rodents. *Trypanosoma congolense* (*T. simiae* ?) was found in 1 of 6 elephants. There were no significant differences in the rates of infection between young and adult animals nor between the sexes. The rate varied with the season, being highest in March and April, the time of heavy rain, and it varied also from year to year in correlation with annual variation in the proportion of infected wild tsetse flies. The animals were far more often infected with *T. congolense* and *T. vivax* than with *T. brucei*, the rate of the last being less than 1 per cent.

Wild tsetse flies, *Glossina swynnertoni* and *G. pallidipes*, were dissected and examined and the following rates of infection with trypanosomes were found among 35,112 flies: *T. congolense* 2·2 per cent., *T. vivax* 2·1 per cent. and *T. brucei* less than 0·1 per cent. The author found (unpublished work) that temperature markedly affected the transmissibility of *T. rhodesiense* and *T. congolense*. The activity and hunger cycle of tsetse flies and their apparent and actual numbers were also investigated.

The erythrocytes of blood recently imbibed by 1,600 *G. swynnertoni* were measured and the results indicated that this species feeds largely on giraffes and large antelopes; some observations by the author [this *Bulletin*, 1944, v. 41, 1010] showed that *G. pallidipes* preferred to feed on pigs.

Various captive wild animals were experimentally infected with *T. rhodesiense*; wart-hogs rarely showed trypanosomes in the blood, but rats were infected from them by inoculation. Trypanosomes appeared in the blood of elands for several days at a time up to 6 months after the infecting bite and a goat was infected by inoculation of 50 cc. of blood from an eland infected 2 years previously. Other animals showed various degrees of infection. *J. F. Corson*

WILDE, J. K. H. **The Maintenance of Cattle under Conditions of Tsetse Fly Infestation in the Field.** *J. Comp. Path. & Therap.* 1947, Oct., v. 57, No. 4, 294–300, 1 sketch map.

This experiment was made to see whether cattle could be kept in good health by the use of drugs in a district in Tanganyika Territory where clearing work to get rid of tsetse flies was in progress, but would not be able to eliminate the flies for a long time; it also served to test the value of two drugs—No. 897 (a compound of phenanthridinium chloride) and Stibophen (antimosan). The experiment began in September 1944 and lasted for 14 months.

A number of cattle (153) were divided into 5 herds (A, B, C, D & E) which were then stationed at 5 different places respectively in the area; their blood was examined microscopically every fortnight for trypanosomes and the drugs were used prophylactically and to treat infections. In herd A (11), infected animals received Stibophen twice with a week's interval between the doses; in herd B (31), infected animals received one dose of No. 897; herd C was subdivided into groups a, b and c for treatment, but all were kept together; in a (15), all got Stibophen once a month, in b (16), all got No. 897 once a month, and in c (15), infected animals got No. 897 after each fortnightly positive blood film; in herds D (25) and E (40), No. 897 was given only when a blood film was positive.

Infections were arbitrarily called new, as distinguished from relapses, if a positive blood film had been preceded by two fortnightly negative films.

Infections with *T. brucei* were not included as this trypanosome appears very irregularly in the blood of cattle and the drugs used are not very suitable for it.

After 14 months, all the remaining cattle were in excellent condition and had increased considerably in weight; no deaths could be attributed to trypanosomiasis or the action of the drugs. No. 897 caused no permanent lameness, though repeated injections produced some local swelling and induration and in one case a cold abscess developed.

The details and results are shown in a table: herd A—10 infected, 1 five times; herd B—23 infected out of 29 (originally 31); herd C—(a) 9 infected out of 14; (b) 4 infected out of 14; (c) 8 infected out of 15; herd D—22 infected out of 25; herd E—17 infected out of 38. The incidence of *T. brucei* was high in herds A, B and D.

No statistical difference in effectiveness was found between the drugs, but it was thought that No. 897 was rather more effective. It was impracticable to leave a control group untreated as experience in Tanganyika Territory has shown that many animals would have died of trypanosomiasis. Prophylactic treatment is more expensive than therapeutic treatment and the only practical way to keep cattle in a tsetse-infested area is to treat the infected animals.

The incidence of infection was very closely related to the number of tsetse flies in the same area, as determined by the Tsetse Research Department.

J. F. Corson

ROMÁN P., J. Contribución al estudio de la epidemiologia de la enfermedad de Chagas en Bolivia. [**The Epidemiology of Chagas's Disease in Bolivia.**] *Rev. Chilena de Hig. y Med. Preventiva.* 1947, Mar., v. 9, No. 1, 61–81, 2 figs. on 1 pl. [13 refs.]

The author puts on record the results of examination of four districts in Bolivia and of the Triatomidae caught in the dwellings. The chief test made was that of xenodiagnosis and, in a considerable proportion, serological reactions. (1) In Colcapirhua, a rural district 10 kilometres east from Cochabamba, 371 persons were examined (166 males, 205 females) and 64 (17·3 per cent.) were positive; of the males 35 (21 per cent.), of the females 29 (14·1). In the same district, 33 dogs and 9 cats were examined, 2 of the former and 3 of the latter were found positive. (2) In Vichacla, 385 (186 males, 199 females) were examined and 32 (8·3 per cent.) were positive, 20 (10·7) of the males, 12 (6·0) of the females. Of 17 dogs, 2 were positive, but none of 8 cats. (3) In San Benito, 73 (33 males, 40 females) were examined and 17 were positive, 10 males, 7 females. (4) In South Yungas, 132 (73 males, 59 females) were examined; 3 males and 6 females were positive, together 6·8 per cent. *Triatoma infestans* was the only transmitter found.

H. Harold Scott

HAUSCHKA, T. S. **Sex of Host as a Factor in Chagas' Disease.** *J. Parasitology.* 1947, Oct., v. 33, No. 5, 399–404, 2 figs.

With mice of four strains, the susceptibility of males and females to three strains of *Trypanosoma cruzi* was compared. The mice used for the study were of uniform genetic constitution, age and weight. One strain of *T. cruzi* was extremely virulent, usually killing mice within three weeks. Infected blood drawn from the heart was diluted with physiological saline, each mouse receiving subcutaneously 0·1 cc. containing about half a million trypanosomes. Culture forms were injected intraperitoneally in 0·5 cc. containing 30–40 million crithidial forms of the parasite. The male mice were more susceptible than

female mice as judged by trypanosome population in the blood, degree of tissue infection, loss of body weight and survival of the host. *C. M. Wenyon*

MUNIZ, J. & DE AZEVEDO, A. P. Novo conceito da patogenia da "doença de Chagas" ("Trypanosomiasis Americana"). Inflamação alérgica granulomatóide (A), e miocardite hiperérgica (B), produzidas em "Rhesus" ("Macaca mullata"), inoculados com formas mortas de cultivo do "Schizotrypanum cruzi". (Nota prévia.) [**New Conception of the Pathogenicity of Chagas's Disease.**] *Hospital.* Rio de Janeiro. 1947, Aug., v. 32, No. 2, 165–83, 8 figs. [22 refs.] English summary.

The authors have studied the pathogenicity of *Trypanosoma cruzi* by sensitizing two monkeys by intravenous injections of a protein-free antigen and then administering a shock injection. The antigen was prepared from cultures grown on solid medium. After the flagellates were washed with saline solution they were dried at a temperature of —70°C. They were kept dry at a temperature of —10°C. or in suspension in distilled water.

To carry out the test, two rhesus monkeys received five intravenous injections of the antigen at intervals of 3 days, two of the injections being 0·040 gm. and three 0·045 gm. Twelve days after the last injection, a shock injection of 0·010 gm. of antigen was given directly into the pleura and the cardiac region. One of the animals was given three further injections of the sensitizing antigen. One of the monkeys was killed eight days after the shock injection and the other 33 days after. Before being sacrificed, both monkeys gave ++++ precipitin reaction according to the method of Muniz and Freitas. As controls, two monkeys were given injections of antigen without a shock injection.

Examination of the pleura and cardiac tissues of the monkeys showed that inflammatory reactions were set up, there being a similarity of the histopathological picture to the lesions in Chagas's disease. In the control monkeys, such lesions did not occur. The experimental result supports the conclusion of TORRES that there is an allergic condition in the pathogenesis of the disease.

C. M. Wenyon

VALLS, D. J. Contribuciones al estudio de la enfermedad de Chagas. VI. Estudio cardio-vascular de enfermos de trypanosomiasis Americana. [**Chagas's Disease. Cardiovascular Study.**] *Rev. Chilena de Hig. y Med. Preventiva.* 1947, June, v. 9, No. 2, 189–249, 7 figs. on 6 pls. [53 refs.]

In this study, the author first carried out xenodiagnostic tests; any persons found positive were then examined clinically to exclude those with other common causes of cardiac disturbance, valvular lesions, arterial hypertension, hyperthyroidism, etc. The districts where the examinations were carried out were rural and heavily infested with Triatomidae.

The author analysed 411 cases [so stated repeatedly, but in a table giving the age and sex of the patients the total should be 417; the numbers of males in one district, San Enrique, being wrongly added and in another column the age distribution total is again wrong]. Of 397 electrocardiograms, there were 123 with sinus arrhythmia, 11 with A.V. block, 6 with ventricular extrasystole (most of these patients were young, 4–18 years of age), and 5 with auricular extrasystole. In spite of this, there seemed to be little, if any, general disturbance of health or limitation of capacity to work. Details are given of 16 cases and in an appendix a general scheme is laid down for clinical study of Chagas's disease noting the points to be looked for and the various laboratory tests to be carried out (xenodiagnosis, Machado reactions, etc); autopsies should be made when permitted, otherwise viscerotomy samples should be taken. *H. Harold Scott*

AUGUSTINE, D. L. **Experimental Studies on Trypanosomiasis** (*Trypanosoma lewisi*). *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 63–80, 3 figs.

The substance of this paper appeared in an earlier publication by the author [this *Bulletin*, 1946, v. 43, 1025]. *C. M. Wenyon*

CALDWELL, F. E. & GYÖRGY, P. **The Influence of Biotin Deficiency on the Course of Infection with** *Trypanosoma lewisi* **in the Albino Rat.** *J. Infect. Dis.* 1947, Nov.–Dec., v. 81, No. 3, 197–208, 1 fig. [25 refs.]

It has been shown by various workers [this *Bulletin*, 1943, v. 40, 825, 891 ; 1944, v. 41, 651 ; 1945, v. 42, 540, 864] that the course of a protozoan infection may be modified by deficiency of certain vitamins in the host. The effect of biotin deficiency on the course of *T. lewisi* infection in rats has now been further investigated by the present authors. To produce this deficiency, one group of animals was given a modified egg-white diet supplemented by other vitamins. Another group received a linoleic acid diet involving a toxic factor and a low protein intake which was also supplemented by other vitamins and did not increase susceptibility to *T. lewisi* infection. The degree of biotin deficiency was assessed from the appearance of the animals. A standard number of trypanosomes, based on body weight, was used for inoculation. Red cell as well as parasite counts were made regularly up to some days after the disappearance of parasites. Death from bacterial and other causes was common in the deficient groups, and all had more severe infections than the controls, while death from very intense infections occurred in moderately deficient rats. When adequate amounts of biotin were given subcutaneously to the latter, the development of trypanosomes was not immediately controlled. Excess biotin given to normal rats likewise exerted no protective or curative action. Treatment with hyperimmune serum caused the trypanosomes to disappear within 24 hours in non-deficient rats, but not in the deficient rats, which later succumbed to the infection ; a deficiency of complement in their serum was indicated. The results suggest that biotin deficiency caused delayed and diminished production of ablastin as well as of trypanolysin, so that an intense and prolonged infection resulted. *J. D. Fulton*

DEANE, Maria P. Ocorrência do *Trypanosoma conorrhini* em " barbeiros " e em rato na cidade de Belém, Pará, e seu cultivo em meio de NNN. [**Occurrence of** *Trypanosoma conorrhini* **in " Kissing-Bugs " and a Rat in Belém, Pará, and its Cultivation on NNN Medium.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, July, v. 1, No. 2, 433–48, 70 figs. on 6 pls. English summary.

The " kissing-bugs " in question, which were found in houses in the " Cidade Velha " section of Belém, Brazil, were identified as *Triatoma rubrofasciata*. Faecal material from the insects revealed the presence of a trypanosome which was proved, by inoculation of white mice, to be *T. conorrhini*. The same infection was found by xenodiagnosis in a live rat caught in a house infested with the infected bugs, although no trypanosomes were found in fresh blood preparations from the rat. In addition to trypanosomes in faecal material of bugs which had fed on the rat, typical trypanosomes were also found in the blood of mice infected by inoculation of such material.

Trypanosoma conorrhini was cultured readily on NNN medium from the blood of laboratory-infected mice and rats and from the naturally infected rat, even when direct examination of the blood was negative.

The author points out that as *Triatoma rubrofasciata* and other *Triatomidae* are frequently infected naturally with *Trypanosoma conorrhini*, this fact should be kept in mind, by those working on Chagas's disease: preferably, when xenodiagnosis is being performed on wild or domestic animals, in the search for *Trypanosoma cruzi*, laboratory animals should be inoculated with the flagellates found in the intestines of the bugs, so that the blood parasites might be identified with certainty. *H. J. O'D. Burke-Gaffney*

LEISHMANIASIS

DORE, G. Maria. Contributo alla conoscenza della leishmaniosi in Sardegna. [**Observations on Leishmaniasis in Sardinia.**] *Pediatria.* 1947, v. 55, Nos. 1/3, 109–15. [24 refs.] English summary (3 lines).

MONDINI, E. M. La leishmaniosi interna della Provincia di Palermo. Rilievi statistico clinici e considerazioni sulla terapia. [**Visceral Leishmaniasis in the Province of Palermo. Clinical Incidence and Observations on Treatment.**] *Pediatria.* 1940, July, v. 48, No. 7, 465–79.

GUIDERI, G. Sulla diffusione della leishmaniosi viscerale infantile nell'Arcipelago Toscano (8 casi osservati negli anni 1945–46). [**Infantile Kala Azar in the Tuscan Archipelago.**] *Acta Med. Italica.* 1947, Oct., v. 2, No. 10, 330–33. [10 refs.] English summary (4 lines).

The author describes eight cases of infantile kala azar which he observed in the hospital of Portoferraio during 1945–6. Seven of these were from the Island of Elba and one from the Island of Pianosa. *C. M. Wenyon*

GATTO, I. Lo splenogramma nel kala-azar nostrano. [**The Splenogram in Infantile Kala Azar.**] *Settimana Med.* 1946, Sept. 7–28, Year 34, n.s., v. 2, Nos. 36/39, 105–12, 1 fig. [16 refs.]

The study of spleen smears from 28 cases of infantile kala azar has revealed the following cell types:

Haemohistioblastic cells, divisible into indifferent haemohistioblasts and lymphoid or haematic haemohistioblasts; plasma cells, monocytic cells, divisible into histioendothelia, lymphoid and haemocytoblastic cells; lymphocytic cells, medullar cells, divisible into granuloblastic and erythroblastic cells. The origin of these various cells from one original splenoblast is shown in the form of a tree. The variations in the occurrence are discussed and the changes undergone by them during treatment are noted. The differential counts before and during treatment are given in two tables. The various cell types are illustrated in a series of photomicrograms. *C. M. Wenyon*

MURANO, G. La splenomegalia leishmaniotica nel quadro delle sindromi bantiane. [**Leishmanial Splenomegaly in the Banit Syndrome.**] *Pediatria.* 1944–45, v. 52/53, 1–52, 1 chart & 5 figs. [77 refs.]

In this article the author describes a fatal case of infantile kala azar in which the post-mortem appearances showing cirrhosis of the liver and spleen are suggestive of Banti's disease. He discusses various observations which have been made and concludes that leishmaniasis is one of the factors which may produce the Banti syndrome. *C. M. Wenyon*

MURANO, G. Polipeptidemia ed azotemia nella leishmaniosi interna. [**Polypeptidaemia and Azataemia in Visceral Leishmaniasis.**] *Pediatria.* 1941, Dec., v. 49, No. 12, 636–53. [38 refs.]

CARNEVALE, A. Sull'importanza dei fenomeni interferenziali nell'associazione lue-leishmaniosi. [**Syphilis obstructing Treatment of Kala Azar.**] *Pediatria.* 1943, May, v. 51, No. 5, 145–55. [22 refs.]

In describing four cases of infantile kala azar which resisted treatment with tartar emetic, the author noted that there was a concomitant syphilitic infection. Response to tartar emetic was only obtained after a course of treatment for syphilis had been completed. He considers that a syphilitic infection should be suspected in all cases of kala azar which resist antimony treatment.

C. M. Wenyon

ROUMAGOUX, J. Un cas de bouton d'Orient autochtone à Mecheria (Hauts-Plateaux oranais). [**An Autochthonous Case of Oriental Sore in Mecheria.**] *Arch. Inst. Pasteur d'Algérie.* 1947, Sept.–Dec., v. 25, Nos. 3/4, 196–8. [Refs. in footnotes.

The first case reported from Mecheria, Oran, at an altitude of 1,167 metres.

See also p. 447, NESS, BRADY, COWIE & LAWTON, **Anomalous Distribution of Antimony in White Rats following the Administration of Tartar Emetic.**

FEVERS OF THE TYPHUS GROUP

ROY, H. K. & BHATTACHARJEE, R. C. **Typhus Fever amongst the Civilian Population in Calcutta. (With a Report of Three Fresh Cases.)** *Calcutta Med. J.* 1947, July & Aug., v. 44, Nos. 7 & 8, 164–5; 190–94, 3 charts.

MONTOYA, J. A., OSEJO, P. P. & TOPPING, N. H. **Typhus in Colombia: a Survey of Four Towns by the Complement Fixation Test, November 1946.** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 163–71, 1 fig. [10 refs.]

The authors employed a complement-fixation test, in which *Rickettsia prowazeki* was used as the antigen, in a study of the sera of 966 persons between the ages of 5 and 49 years in four villages of South Colombia. The villages were about 3,000 metres above sea level, the average air temperature was about 11–12°C., and the conditions of life were suitable in all respects for the maintenance of louse-borne typhus infection.

About 25 per cent. of the sera gave positive reactions at titres of 1–8 or more and it was concluded that at least as great a percentage of the inhabitants had been attacked at some time with typhus fever.

The antigen used was not purified so as to differentiate between louse-borne and flea-borne typhus, but the epidemiological conditions described in the paper strongly suggest that the infection was louse-borne.

It is stated that there was no clear evidence that age or sex caused a statistically significant difference in the incidence of the disease, and that the incidence rates did not show peaks which could be considered as due to the occurrence of epidemics.

John W. D. Megaw

KUBICZ, J. **Techniques for Rickettsial and Virus Cultivation.** *Proc. Soc. Exper. Biol. & Med.* 1947, Oct., v. 66, No. 1, 186–7.

The technique described refers to the rearing of human body lice in sterile conditions for use in feeding experiments on patients suspected of being infected with virus and rickettsial diseases. Freshly hatched larvae, reared from eggs laid by laboratory-bred lice which have to be fed twice daily on healthy persons, are fed on the patient in aseptic conditions twice daily for 4 to 12 days; the infecting organisms are sought in stained smears of the faeces and guts of the insects. Details of the technique are given.

The author states that he has " isolated and observed the infectious bodies responsible for a number of virus and rickettsiae-like diseases ". The bodies are said to have been, for the most part, round disks about the size of typhus rickettsiae and to have been causally associated with several diseases of a rheumatic type, including acute rheumatism and chorea minor. In one case, the disease was a toxic diarrhoea in an infant.

Larval bedbugs were reared in the same way and in some cases gave better results than louse larvae.

[It seems strange that the bodies seen in virus diseases should have been similar to those observed in rickettsial infections. The information supplied with regard to the practical application of the method of investigation is tantalizingly meagre. It is to be hoped that this aspect of the study will be dealt with in further communications.

The early part of the investigation was carried out in the Weigl Typhus Institute at Lwow.] *John W. D. Megaw*

GIROUD, P. Pouvoir neutralisant de la streptomycine sur les Rickettsies du typhus épidémique mis en évidence dans la peau. [**The Neutralizing Effect of Streptomycin on Rickettsiae of Epidemic Typhus as shown by Skin Tests.**] *C. R. Soc. Biol.* 1947, Nov., v. 141, Nos. 21/22, 1117–19, 4 charts.

The author studied the effect of streptomycin on rickettsiae of epidemic typhus by intranasal inoculation of mice and by skin tests on rabbits. In the former experiments, 20 anaesthetized mice received 6 drops of a rickettsial suspension and thereafter were given 2,000 units of streptomycin daily: in some cases, 10,000 units were injected on the first day. In a first series of experiments, no rickettsiae were found in the lungs of the treated mice; in a second series, rickettsiae were found in approximately equal degrees in lungs of treated and untreated mice alike. However, in the case of the treated animals, the rickettsiae often stained less readily, took a blue instead of a red colour with Macchiavello's stain and were punctiform. In the control mice, the morphology and staining of the rickettsiae were normal. Evidently the only action of the streptomycin on the rickettsiae was to modify their morphology.

In the skin tests, the skin of rabbits was inoculated with 1 mgm., 2 mgm. and 4 mgm. of lung tissue heavily infected with rickettsiae, mixed with solutions of streptomycin containing from 1·8 units to 18,000 units. The suspensions and the dilutions of streptomycin were kept in contact for 1 hour at 30°C. Neutralization of the rickettsiae was assessed in terms of the delay or feebleness of the local reactions produced. A chart and a table in the text indicate that 1,800 and 18,000 units completely neutralized the rickettsiae up to the 4 mgm. quantities of infected tissue: the smaller doses had a correspondingly weaker effect, and 18 units only neutralized 1 mgm. completely, while 1·8 units had little effect.

The author concludes that streptomycin has a definite effect on typhus rickettsiae when tested intradermally, but this is less in evidence in the case of experimental pulmonary infection. *H. J. O'D. Burke-Gaffney*

TUNA, I. Yerli ve yabanci tifüs aşilarinin muafiyet kudretlerinin karşilikli mukayeseleri. [**Comparison between the Antigenic Power of Typhus Vaccines prepared in Turkey and elsewhere.**] *Türk. Ijiyen Tecrübî Biyoloji Dergisi.* Istanbul. 1945, v. 5, 107–14. [18 refs.] French summary.

In the author's laboratory at the Central Institute of Hygiene in Refik Saydam, typhus vaccine was prepared during the war by the cultivation of rickettsiae in the egg embryo (Cox.) In the present investigation, the antigenic power of this vaccine was compared in guineapigs under carefully controlled conditions with vaccines from seven other prominent sources in Europe and the United States. The results are tabulated ; and although not more than 10 guineapigs were used in any one test, it is claimed that the Refik Saydam vaccine was as active as the others, on the basis of the number of guineapigs successfully immunized with it. *H. J. O'D. Burke-Gaffney*

COLE, L. C. & KOEPKE, Jean A. **Problems of Interpretation of the Data of Rodent-Ectoparasite Surveys and Studies of Rodent Ectoparasites in Honolulu, T.H., Savannah, Ga., and Dothan, Ala.** *Supplement No. 202 to Pub. Health Rep.* Wash. 1947, 71 pp. 3 figs. & 3 maps. [63 refs.]

In the first part of this report, the authors discuss the complexities to be considered in applying the " flea-count " technique to investigations into the populations of rodent ectoparasites. The chief object of such surveys being to obtain an index from the raw data which will bear an approximate relationship to the total ectoparasite population sampled, it is essential that several factors which complicate such studies should be borne in mind.

Some of the points discussed include the accurate identification of species of ectoparasites and their hosts, their sex and age ; food of the host ; location of traps ; number of traps ; number of rats per trap ; efficiency of the traps and of the trappers ; and many more. The meaning and limitations of different types of indices are considered, in particular, the mean number of fleas per rat ; mean *Xenopsylla cheopis* per rat ; mean female *cheopis* per rat and corresponding indices for infested rats. The mean number of female *cheopis* per infested rat is probably the most promising of these indices for evaluating the effect of control measures, because normally it is the least variable; but the reader is warned that this index cannot yet be justified for use with other species.

It is pointed out that in different places, different factors may take precedence in influencing the index. The survival of fleas away from their hosts is promoted by low temperature and ample moisture, but a high temperature induces more frequent feeding and increases the proportion of males in the catches. However, as the value of the vector-count technique seems to have been established it may perhaps merit extension into other fields of enquiry. For instance, it may be found that vector indices correlate more closely with enzootic typhus than with human typhus and more closely with the microclimate of the rat-holes than with data from weather stations, but these are subjects for special investigation and are not measurable from the data available in these reports.

The results of a survey of rodent-ectoparasites of Honolulu are then considered. Trapping of rodents began in January 1934 and ended in January 1935. Results for 282 days catches are analysed. Of 6,664 rats, 4,967 (74·5 per cent.) were

Rattus norvegicus, 1,238 (18·6 per cent.) were *R. rattus* and 459 (6·9 per cent.) were *R. hawaiiensis*. The fleas from 6,382 of these rats numbered 41,402; *Echidnophaga gallinacea* formed over 59 per cent. and *Xenopsylla cheopis* over 39 per cent.; other fleas taken were *Ctenocephalides felis* and *X. hawaiiensis*. The number of mites taken from 666 rats (a 10 per cent. sample) was 6,530; among them *Laelaps hawaiiensis* accounted for over 91 per cent., *Echinolaelaps echidninus*, 8 per cent. and *Liponyssus bacoti* 0·4 per cent. Lice from the sample 666 rats were 2,380 and of these *Polyplax spinulosa* amounted to over 82 per cent. and *Hoplopleura* spp. to over 17 per cent.

The figures are analysed in a dozen tables and from these it is seen that *R. hawaiiensis* had significantly fewer lice and fleas than *R. rattus*, and the latter had fewer fleas than *R. norvegicus*. Mites occurred indiscriminately on the different rats. The mite *L. hawaiiensis* was abundant in the wet season and the flea *X. cheopis* was most prevalent in the dry season. Certain aspects of these results seem to warrant further careful investigation, for the mite *L. hawaiiensis* was apparently more abundant than the flea *X. cheopis*, and the mite *L. bacoti* (a laboratory vector of rodent typhus), was comparatively rare; moreover, the survey shows that human incidence of typhus coincided more closely with the peak abundance of *L. hawaiiensis* than with that of *X. cheopis*. These findings demonstrate the necessity for ectoparasite surveys in different places, at different times and under a variety of conditions.

The results of similar work in Savannah, Georgia, are next analysed in the same way except that all rats (rather than a 10 per cent. sample) are included in the examination for mites and lice as well as for fleas. Trapping was done from January 1932 to December 1933, during 617 trapping days. Here *R. norvegicus* formed over 90 per cent. of the total rat collection (7,813 rats) while less than 7 per cent. were *R. rattus*. The situation here appears to be even more complex, because, though Savannah is regarded as a city with a relatively high incidence of endemic typhus, this is not associated with any peculiar qualitative features disclosed by the analysis of the survey figures. The mite *L. bacoti*, while more abundant here than in other cities surveyed (33,496 or 45 per cent.) failed to show the seasonal variations characteristic of this disease. The data for Savannah offer little information except that important ectoparasites were found. These were those named above, with the addition of *Leptopsylla segnis* (a flea which was more closely associated with *R. rattus* than with *R. norvegicus*), and some other less abundant species.

The last part of the report deals with surveys at Dothan, Alabama, which is not a seaport. Rat collections were made from March 1933 to March 1934, during 317 trapping days. The figures analysed are those from 4,832 rats, of which *R. norvegicus* made up about 86 per cent. and *R. rattus* 0·7 per cent. Of 51,005 fleas, *X. cheopis* accounted for over 48 per cent., *E. gallinacea* over 28 per cent. and *L. segnis* over 21 per cent. Of 15,231 mites, *E. echidninus* was easily the commonest, with over 91 per cent.; and of the lice (8,900), over 93 per cent. were *Polyplax spinulosa*.

The results from the Dothan survey contrast with the results from other places. The area is one of high incidence of endemic typhus, and because of the low figures for *R. rattus* (45) and the mite *L. hawaiiensis* (6) neither of which appear to be essential for transmission, and because *P. spinulosa* and *E. gallinacea*, though numerically adequate, show variations inconsistent with typhus epidemiology, suspicion is therefore directed to *X. cheopis*.

H. S. Leeson

See also p. 425, WANSON, RICHARD & TOUBAC, **Les rongeurs et insectivores de Léopoldville et leurs ectoparasites.**

BERTAZZI, C. G. Ulteriore contributo alla terapia del dermotifo murino della Sicilia orientale mediante l'uso del chinino e della maretina. [**The Treatment of Murine Typhus in Sicily with Quinine and Maretine.**] *Acta Med. Italica.* 1947, Dec., v. 2, No. 12, 383–6, 2 charts. English summary.

An account of two cases with apparently good results.

WILEY, J. S. **A Preliminary Report concerning DDT Dusting and Murine Typhus Fever in Nine South-eastern States.** *Pub. Health Rep.* Wash. 1948, Jan. 9, v. 63, No. 2, 41–3, 1 fig.

In July, 1945, the U.S. Public Health Service inaugurated a typhus control programme in 9 south-eastern States, in collaboration with the State Health Departments. The work was continued throughout 1946 and the first half of 1947. The programme involved primarily the application of 10 per cent. DDT dust to rat runs, burrows and harbourages in an attempt to reduce rat fleas and other ectoparasites and so to control human murine typhus fever.

This work was carried out in 122 of the highest typhus reporting counties in the 9 States, which between them had accounted in 1944 for 72·3 per cent. of all typhus reported in these " typhus " States or 70·5 per cent. of all typhus reported in the entire U.S.A.

A table and a figure show the results of these dusting operations, tabulating separately the figures from the 122 counties which operated the dusting projects and those from the 460 counties which did not. The year 1944 is also shown as a " precontrol " year.

These results show that in the period July–December 1945 a decrease in reported typhus of 10·7 per cent. occurred in dusted counties compared to an increase of 14·5 per cent. in the non-dusted counties, a differential of 25·2 per cent. In 1946 and half of 1947 the differentials were 44·1 per cent. and 56·4 per cent.

The reported cases decreased in the 10 highest " typhus " counties from 1,074 in 1944 to 395 in 1946. In tabulating the results, DDT dusting is the only control measure taken into account.

In the treated areas, flea counts from some 17,000 live rats have indicated that *X. cheopis* reduction has averaged 84 per cent.

H. J. O'D. Burke-Gaffney

BETTINARDI, G. La febbre esantematica mediterranea. [**Mediterranean Exanthematic Fever.**] *Pediatria.* 1942, Sept., v. 50, No. 9, 343–52.

The author presents a critical summary of the extensive literature connected with the tick-borne typhus fever which occurs in the countries round the Mediterranean Sea, and which has been described under such names as boutonneuse fever, escharo-nodular fever, eruptive Mediterranean fever, Carducci's disease, benign " non-diffusible " dermo-typhus, Marseilles fever, etc.

The paper contains much information that will be found useful by students of the typhus fevers though some of the author's statements may be misleading to the uninitiated reader ; for example, flea-borne typhus is constantly referred to as Brill's disease. Stress is rightly laid on the doubt that exists as to whether all the cases described as belonging to the Mediterranean exanthematic fever sub-group have been correctly diagnosed ; neither the Weil-Felix reaction nor the response of guineapigs to inoculation can always be relied on to differentiate the disease from murine typhus.

In clinical diagnosis special importance is attached to the rash, which in most cases appears between the 2nd and 4th day, and when fully developed consists

of discrete papules, or even nodules, and tends to be widely distributed, extending to the face, palms and soles. Constanzi is quoted as saying that an eschar occurs in 30 per cent. of the cases. *John W. D. Megaw*

PHILIP, C. B. **Comments on the Name of the Q Fever Organism.** *Pub. Health Rep.* Wash. 1948, Jan. 9, v. 63, No. 2, 58.

In this brief note the author produces arguments to support the use of the name *Coxiella* for the aetiological agent of Q fever, *R. burneti*. He has been using the name as a full genus for teaching and other purposes during the war. " It is here proposed to validate that usage by elevating *Coxiella* to the status of a full genus, the genotype, of course, remaining the same, *i.e.*, *R. burneti* Derrick, which now becomes *Coxiella burneti* (Derrick)."

H. J. O'D. Burke-Gaffney

SMADEL, J. E., SNYDER, M. J. & ROBBINS, F. C. **Vaccination against Q Fever.** *Amer. J. Hyg.* 1948, Jan., v. 47, No. 1, 71–81, 1 fig. [22 refs.]

The authors, working at the U.S.A. Army Medical Centre at Washington, D.C., prepared vaccines from yolk-sac cultures of an Italian (Henzerling) and an American (Dyer) strain of *Rickettsia burneti*. A concise description is given of the methods employed in preparing and testing the vaccines.

Guineapigs inoculated with either of the strains of vaccine showed a rapid rise in the complement-fixation titre for the Italian strain of antigen, starting about two weeks after inoculation ; but the rise in the titre for the American strain of antigen did not occur till about four weeks after inoculation. After about eight weeks the titres for both strains of antigen were approximately equal.

Guineapigs that were already positive for the Italian strain, but had not become positive for the American strain, appeared to have acquired the same high degree of relative immunity against both strains of infection as was shown by the guineapigs positive for both strains of antigen.

Among 28 volunteers inoculated with the Italian strain of vaccine, 23 gave complement-fixation titres of 1–20 or more when tested two weeks later with Italian antigen, but all were negative to tests with American antigen.

Among 11 volunteers inoculated with the American strain of vaccine, seven reacted at 1–20 or more to tests with the Italian antigen, but only one reacted with the American antigen.

By later tests it was found that few of the volunteers ever developed complement-fixing antibodies for the American strain and that only two failed to develop antibodies for the Italian strain though in a few cases the titres were only 1–5 or 1–10.

There was no opportunity for testing the efficacy of the vaccines against human infection. *John W. D. Megaw*

YELLOW FEVER

KIRK, R. **Extermination of *Aëdes aegypti* in Khartoum.** [Correspondence.] *Nature.* 1948, Jan. 24, 139.

The author, writing from the Stack Medical Research Laboratories, Khartoum, refers to an editorial note in *Nature*, 1947, August 9th, 186, in which it is stated that yellow fever has been exterminated from Khartoum as a result of mosquito control measures. He points out that while *Aëdes aegypti* has been

virtually eliminated in Khartoum, there is in fact no evidence of actual yellow fever infection ever having been identified there. Khartoum is north of the local yellow fever endemic area and immunity surveys show no evidence of infection having occurred during the life-time of the present inhabitants.

Since the successful anti-mosquito campaigns of BALFOUR some forty years ago, the mosquito situation in Khartoum has been observed constantly: records over that period suggest that *A. aegypti* has never been very abundant in that desert neighbourhood and has been eradicated, to reappear infrequently and be rapidly destroyed. Such reappearances in the past were probably re-importations, since the mosquito at one time was regularly brought to Khartoum by river steamers: but the great reduction of mosquitoes on steamers is one of the effects of the present mosquito control measures in the Sudan described by LEWIS [this *Bulletin*, 1947, v. 44, 656] whose paper was the subject of the editorial note referred to above. *A. aegypti* has not been reported on those steamers for several years. *H. J. O'D. Burke-Gaffney*

PLAGUE

WANSON, M., RICHARD, P. & TOUBAC, M. Les rongeurs et insectivores de Léopoldville et leurs ectoparasites. [**Rodents and Insectivores of Leopoldville and their Ectoparasites.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1947, July, No. 6, 3–38, 8 figs., 1 chart & 24 photos. [50 refs.]

A list is given of the names of 7 species of *Insectivora* and 26 *Rodentia* found in the Léopoldville area of the Belgian Congo. Among 29,245 domestic rodents examined, no specimen of the brown rat (*Rattus norvegicus*) was seen, but there were four forms of the black rat, namely: *R. rattus* (1,772), *R. alexandrinus* (14,607), *R. frugivorus* (12,854) and *R. wroughtoni* (112). Among 10,461 non-domestic rodents taken outside the town, 22 species were represented, the commonest being the marsh rat *Dasymys bentleyae* (5,689).

Descriptions are given of the animals, their burrows and their nests and a key is provided for their identification. There are also drawings and photographs of certain diagnostic characters, but, unfortunately, some of the names under the photographs of skulls have been misplaced and it has been necessary to insert a correction sheet in the volume.

Among the fleas taken from the domestic rodents, *Xenopsylla brasiliensis* was most common, being taken 29,008 times; *X. cheopis* was collected 13,816 times, *Ctenocephalides felis strongylus* 242 and *Echidnophaga gallinacea* 158 times; maximum numbers were collected in the cool, dry months of August and September. The two species of *Xenopsylla*, though abundant on the rats, were rarely seen in houses. In African huts, *C. felis strongylus* and *Tunga penetrans* were common. *Polyplax spinulosa* was the only louse on the four black rats, though no numbers are given. In the dry season, the mites *Dermanyssus muris* and *Liponyssus bacoti* appeared on *R. alexandrinus*; from 600 rats, 210 *L. bacoti* were taken, the first time this mite has been identified from the Congo. Species of *Laelaps* also occurred, but only averaged 8 mites per 1,000 rats. Nymphs and adults of the tick *Haemaphysalis leachi* were collected but the numbers are not stated.

On 10,409 field and woodland rodents, 80 per cent. carried mites, 1 per cent. fleas and 19 per cent. were free of ectoparasites. The fleas were *X. nubicus*, *X. brasiliensis* and *X. cheopis*; fleas of other genera were absent. Mites of the genus *Laelaps* were common, especially on some specimens of the marsh rat (*D. bentleyae*), which were free of fleas. A few *H. leachi* were obtained and

some *Rhipicephalus simus* and *R. sanguineus*. At the mouths of the burrows, *Phlebotomus schwetzi*, *P. africanus*, *Mansonioides africanus*, *M. uniformis* and *Culex fatigans* were taken on oiled paper traps. *H. S. Leeson*

ERZIN, N. & PAYZIN, S. Akçakale vebasi. [**Plague in Akçakale.**] *Türk Ijiyen Tecrübi Biyolojî Dergisi*. Ankara. 1947, v. 7, No. 3, 31–44, 2 figs. & 1 folding chart. English summary.

In March–April, 1947, 19 cases of plague occurred in Akçakale, Turkey: 14 were axillary bubonic and 5 were septicaemic. Plague serum from the Pasteur Institute (80 cc. daily) was not satisfactory, but sulphonamides proved of great value in treatment; in some cases these drugs were combined with serum therapy.

Serum and sulphadiazine were given prophylactically to 8 relatives of patients: they did not develop the disease, but four persons who refused this treatment developed typical bubonic plague. As an insecticide "6 per cent. DDT in petrol" was very satisfactory. *H. J. O'D. Burke-Gaffney*

FAUST, E. C. **Plague in the Americas.** *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 213–24, 2 figs. (maps). [17 refs.]

Plague in the Americas has been well reviewed in a large number of publications and the history of its introduction to the American continent in 1899 by the Dutch ship *Zeir* should be well known. In this article there is reference to the accepted view of how plague became established in ground squirrels. The San Francisco disaster of 1906 resulted in the escape of city rats from the Chinese slums into the hills and the transference of their fleas to the squirrels. In continuation of this explanation there comes the author's view that 'it can never be proved that this so called "sylvatic plague" did not exist prior to the San Francisco earthquake and even before the introduction of rat plague from China'. [Could this be comparable to the existence of endemic plague in the Kumaon hills of British India before its arrival at Bombay from Hong Kong ?]. The author considers that plague, exclusively in domestic rats, could be eradicated, but that the danger remains of reintroduction to the rat population of the infection from the enzootic plague of wild rodents. His views on the transmission of plague in South America may be contested when he says that, "if the domestic rat was the original reservoir among these peoples, it has ceased to be important, for the disease is to-day transmitted by human rather than rodent ectoparasites", that is to say by the human flea or even lice and from man to man. *W. F. Harvey*

CHOLERA

BIRAUD, Y. & KAUL, P. M. **World Distribution and Prevalence of Cholera in Recent Years.** *Epidemiological & Vital Statistics Rep. W.H.O., Interim Commission.* 1947, Dec., v. 1, No. 7, 140–54, 3 charts & 1 map. [In parallel French & English.]

This document on the recent cholera epidemic in Egypt is of great importance, coming as it does from the World Health Organization of the United Nations. In its explanation of the origin of the epidemic it follows standard and regulation lines. If that explanation is not wholly acceptable, it simply means that ignorance still prevails on the subject of cholera, not so much perhaps on its epidemiology as on its endemiology.

The epidemic was unexpected, and it is stated categorically that, 'Cholera still fully deserves its qualification of "Asiatic" . . . because for the last thirty years it has been confined to that continent'. There is abundant evidence that India is the most persistently affected part of Asia, but we learn that figures for British India are more reliable than elsewhere and that British India up to 1947 contained some three-fourths of the population of India. Prominence of the cholera of British India may have something to do with the reliability of its statistics. By British India is meant, for the most part, the Gangetic Valley and the city of Calcutta, although in the present case attention is directed rather to the Punjab. Particular note is taken in this publication of those correlated factors in epidemic cholera :—famine, war, pilgrimages and panic-striken populations. In India, the Japanese war menace, the Bengal famine and the large-scale movement of population as a result of partition are rightly noted.

The earliest history of the present epidemic is very interesting, because "the first three cases were believed to be food poisoning," that is to say, presumably, something more severe than subclinical cholera or mild diarrhoea. A very important factor in the subsequent development of the epidemic was that El Korein, the focal point, was overcrowded with a non-resident population : a stampede of this population spread the epidemic first over the lower Nile provinces and then over the upper. Large cities with a chlorinated water supply and satisfactory sanitation escaped very lightly, as one may expect is the position of Europe to-day compared with last century.

Some note may be taken of the record that "the source of the epidemic is still obscure" and that "first-hand observers think they can trace the origin of the infection to Egyptian labourers infected by aeroplanes coming from India." The explanation offered seems to be that of the landing of a germ carrier from India. There is positive evidence that cholera was absent during the Mecca pilgrimage in 1947 and that the epidemic broke out before the return of the pilgrims.

A contention that vaccination of the whole population and the winter season, unfavourable to cholera prevalence, both played their part in the limitation of the outbreak might perhaps be met by opposing the remarkably similar graphs of cholera epidemic for 1902 and 1947. No vaccination can have been instituted in 1902. The longer duration of the epidemic in 1896 might reasonably be given as being due to the season of its occurrence, May to October. We may note also the intention of the authorities to institute a vaccination campaign to cover the entire population in 1948. Practically no mention is made in this account of chemotherapy for cholera, among the highly commendable and energetic activities of the Egyptian authorities.

W. F. Harvey

GALLUT, J. & GRABAR, P. Recherches immunochimiques sur le vibrion cholérique. V. Absence de pouvoir antigénique de la substance hypothermisante de la toxine cholérique. [**Absence of Antigenic Power in the Hypothermy-producing Component of Cholera Toxin.**] *Ann. Inst. Pasteur.* 1947, Nov., v. 73, No. 11, 1139–42.

Two different fractions are demonstrable in cholera toxin, one of large molecule ($d > 100$ mμ), a conjugate protein of glucolipidic type, and another of small molecule ($d < 4$ mμ) of unknown character, but causing hypothermy [this *Bulletin*, 1943, v. 40, 910 ; 1944, v. 41, 401 and 402 ; 1945, v. 42, 807 ; 1946, v. 43, 129]. The first component is identified as cholera O antigen and, as an antigen, furnishes a neutralizing antiserum. This antiserum has no action on the second component. The present research sets out to determine whether

the second component is antigenic and to investigate its specificity. The authors find that it is devoid of antigenic power. *W. F. Harvey*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

REES, C. W. & REARDON, Lucy V. **Problems on the Growth Requirements of the Parasitic Protozoa.** *Liber Jubilaris J. Rodhain (Soc. Belge Méd. Trop., Brussels).* 1947, Dec., 303–25. [80 refs.]

This paper is a review of literature dealing with the cultivation of *E. histolytica*, various Trichomonadidae, pathogenic trypanosomes and leishmania and species of *Plasmodium*, with particular reference to the constituents of the media employed. The various papers referred to have been reviewed in this *Bulletin.* *C. M. Wenyon*

SPINGARN, C. L. & EDELMAN, M. H. **The Prolongation of the Viability of Cultures of *E. histolytica* by the addition of Streptomycin.** *J. Parasitology.* 1947, Oct., v. 33, No. 5, 416–18.

The authors have found that cultures of *Entamoeba histolytica* on Difco amoeba medium covered with horse-serum saline and having rice particles added, progress satisfactorily when subculture is made every 48 hours. Active amoebae can be found in these cultures up to the 8th day. After the addition of 1,000–3,000 units of streptomycin to the serum saline, amoebae grew in most instances ; but after 24 to 48 hours the amoebae were fewer than in the controls, though they appeared to be normal in size and motility and in their power to ingest rice. The average survival time in streptomycin cultures was 33·7 days, in contrast to 8·0 days in controls. Some cultures survived 40 or 50 days and one 70 days. In the streptomycin tubes bacterial growth was markedly inhibited. *C. M. Wenyon*

WRIGHT, A. W. & COOMBES, A. E. R. **Treatment of Amoebic Dysentery** *Lancet.* 1948, Feb. 14, 243–6, 3 figs. [20 refs.]

Not only was the incidence of amoebic infection in India Command double that of the average pre-war rate, but response to treatment was poor.

The importance of early diagnosis became clear. On the day after admission, sigmoidoscopy was done as a routine. A warm stage and warm saline were used and material from rectal or sigmoid swab was immediately examined under the microscope.

Emetine bismuth iodide was frequently given in tablets ; in three patients it was ascertained by radiography that they were not being absorbed. These cases and a number of others similarly treated showed no grey discolouration of the stools, such as is seen after proper administration of E.B.I. Early in the investigation it became apparent that, though fresh cases responded well to a thorough course of treatment, the relapsing cases and those with a long history before treatment did not. A further important factor appeared to be a secondary bacterial infection. Isolation of a pathogenic organism or the finding of a bacillary exudate was taken as evidence of such an infection, which was proved in 41 per cent. of cases. The incidence was not significantly greater in chronic than in fresh cases. On these premises, a course of treatment was devised

consisting of 2 mega units of penicillin and 65 gm. succinyl sulphathiazole followed by E.B.I. and quinoxyl enemata for 12 days and carbarsone for 10. In all, 92 patients were given penicillin. Sigmoidoscopy was carried out before and after this treatment and in every case where ulceration had been seen there was striking improvement.

On the completion of treatment, the patient was retained in hospital for ten days, during which 6 stools were examined and sigmoidoscopy was done. After a period of three weeks in a convalescent depot, he returned to hospital for a week. Three more stools were examined and sigmoidoscopy was repeated. If he was apparently cured, he was discharged and required to report by postcard in three months' time. The importance of sigmoidoscopy is emphasized, as lesions suggesting amoebiasis were present in 88 per cent. of cases with negetative *E. histolytica*.

In 21 per cent. of cases, the organisms were present in the swab when the stool was negative.

Cure was effected in 97·5 per cent. of primary cases with symptoms lasting two months or less ; 96·1 per cent. of all primary cases were cured, 85 per cent. of those with one previous attack, and only 58·4 per cent. of those with more than one attack. *P. Manson-Bahr*

MANSON-BAHR, P. & MUGGLETON, W. J. **The Response of Intestinal Amoebiasis to Diodoquin Treatment.** *J. Trop. Med. & Hyg.* 1948, Feb., v. 51, No. 2, 23–7. [10 refs.]

The authors treated 71 patients suffering from intestinal *Entamoeba histolytica* infections with Diodoquin (Searle). The dosage was two tablets (6·4 grains) four times daily after food for fifteen days. The patients could be divided into four groups as follows :—

Series I.—Six with acute amoebic dysentery. The drug proved valueless in these.

Series II.—Twelve with a history of amoebic dysentery in the preceding five years, but quiescent at the time of treatment. One had an acute clinical relapse within three weeks ; eleven were free from cysts three to sixteen weeks after treatment.

Series III.—Twenty-three with a history of previous diarrhoea. One continued to pass cysts throughout and after treatment ; twenty-two were free from cysts three to 104 weeks after treatment.

Series IV.—Thirty apparently healthy carriers with no history of diarrhoea. All were free from cysts three to 120 weeks after treatment. [Six was the maximum number of stools examined in any one case of the four series.]

There was no evidence of genuine toxic action of the drug in the 71 cases. Sigmoidoscopy or proctoscopy, where these were done, showed typical amoebic ulceration in the Series I cases, a pigskin type of pitting in the Series II and III cases, and a normal mucosa in the Series IV cases.

The nature of the infection in the carrier, or symptomless cyst-passer state, is discussed ; the authors incline to the view that *E. histolytica* lives in the lumen of the bowel, as a coprozoic organism in some cases. This type of infection is eradicated by diodoquin, which is an efficient drug for this purpose as it is dispersed in the intestine, and is not absorbed to any material extent. Cysts of non-pathogenic amoebae, and of *Giardia intestinalis*, when these were present, disappeared after diodoquin treatment but the latter reappeared within two months. *A. R. D. Adams*

CONAN, N. J., JR. **Chloroquine in Amebiasis.** *Amer. J. Trop. Med.* 1948, Jan., v. 28, No. 1, 107–10.

In view of the occasional toxicity of emetine, it is desirable to have available a non-toxic substitute for it in the treatment of amoebic involvement of the liver. Some members of the 4-aminoquinoline series, which have a high antimalarial activity, can be given in a non-toxic dosage which is associated with localization in high concentration in tissues, especially the liver.

The author studied the anti-amoebic activity of one of these compounds, chloroquine [see this *Bulletin*, 1948, v. 45, 37]. He quotes the work of BERLINER *et al.* (in the press) indicating that this drug is localized in the liver of the rat in concentrations 400 to 600 times those in the plasma.

A table shows that, *in vitro*, chloroquine had an amoebicidal activity greater than that of Anayodin and Carbarsone, but less than that of emetine. In human amoebiasis, chloroquine was given firstly as a priming dose to saturate the tissues and rapidly obtain the equilibrium plasma concentration and secondly as sustaining doses for 2 or 3 weeks. The doses used were far in excess of those required for antimalarial activity and were about one-half of the believed minimal toxic dose, as estimated by Berliner *et al.* The priming doses consisted of 0·3 gm. of the base twice daily for 2 days and the sustaining doses were 0·3 gm. daily for 12 or 19 days more: all doses were given orally.

In these experiments, plasma concentrations of the drug were not determined, but from the work quoted above it is indicated that they would amount to about 150 microgrammes per litre. No toxic symptoms were observed, but two patients with amoebic hepatitis had mild and transient gastric symptoms. Altogether, 28 patients with intestinal amoebiasis and 6 with amoebic hepatitis were treated with Chloroquine. Thirteen of the former continued to show parasites in the stools after one course of treatment: the other 15 have had persistently negative stools for 2 to 8 months. The author emphasizes that as the follow-up period lengthens the figures can only change unfavourably.

In the 6 cases of amoebic hepatitis, symptoms and signs disappeared sharply within a few days of the beginning of treatment: they have not recurred within 2 to 12 months.

The drug had no effect on non-pathogenic intestinal protozoa or on a number of species of helminths.

As chloroquine is almost entirely absorbed from the gastro-intestinal tract, its effect on amoebae in the colon must be due to plasma or tissue concentration.

The author states that this report is wholly preliminary and its primary purpose is to call attention to the anti-amoebic activity of this non-toxic drug and to encourage others to test it, especially in amoebic hepatitis.

H. J. O'D. Burke-Gaffney

FULTON, J. D. & JOYNER, L. P. **Natural Amoebic Infections in Laboratory Rodents.** *Nature.* 1948, Jan. 10, 66–8. 6 figs. [10 refs.]

In the course of chemotherapeutic work on *E. histolytica*, the following animals were examined for naturally occurring amoebic infections—white rat, cotton rat (*Sigmodon hispidus*), hamster (*Cricetus auratus*), Orkney vole (*Microtus orcadensis*). In all of these, an amoeba resembling *Entamoeba coli* was discovered in 50–70 per cent. of animals examined. The amoebae and their binucleate cysts are illustrated in microphotographs. Attempts at cultivation of the amoebae failed.

C. M. Wenyon

RELAPSING FEVER AND OTHER SPIROCHAETOSES

GAUD, M. & MORGAN, M. T. **Epidemiological Study of Relapsing Fever in North Africa (1943–1945).** *Bull. World Health Organization* (United Nations). 1947/48, v. 1, No. 1, 69–92, 1 map & 2 charts.

An U.N.R.R.A. Mission consisting of Dr. Gaud and Dr. Morgan proceeded to French North Africa in November 1945 in order to study the epidemic of louse-borne relapsing fever which, after 25 years' quiescence, had spread rapidly through Tunisia, Algeria and Morocco. The last epidemics were in North Africa between 1912 and 1915 and in French West Africa between 1922 and 1925. During the intervening period, only small foci of the tick-borne disease existed.

This study is divided into three parts, epidemiological, clinical and therapeutic. It was shown that the origin of the epidemic was in the Fezzan region of southern Tripolitania. This was also thought to be the reservoir of the virus in the 1912 epidemic by NICOLLE (whom the authors frequently quote and whose work permeates the whole story of relapsing fever). The disease apparently began in the nomad tribe of Megarha, in the last quarter of 1942. Caravans spread the disease throughout the Fezzan and half the population became infected between November 1942 and May 1944, when the infection died out. The neighbouring countries, however, passed on the infection, which eventually reached Morocco in the west. In Tunisia, approximately 400,000 cases occurred (20 per cent. of the population); in Algeria, 432,000 (5 per cent. of the population); in Morocco, perhaps 180,000 cases.

The epidemic was associated with a grave economic crisis, which has long been recognized as an essential precursor of louse-borne epidemics. Contrary to the classical notion that cases should be most numerous in the winter, on this occasion, there was no seasonal trend and the epidemics developed rapidly, irrespective of the season of their inception.

No actual evidence is cited that the louse was the vector of the disease in North Africa, though it was assumed to be so. The rôle of the bed-bug was investigated and work at the Casablanca Pasteur Institute has shown that these insects can become infected by biting an infected person and that they are still infective after the first moult, as can be proved, if they are crushed and injected.

The use of D.D.T. has revolutionized the methods of control, and the systematic use of this insecticide has proved completely efficacious. The inhabitants welcome this method, which they recognize as valuable and harmless. Unfortunately, supplies of this substance do not appear to have been adequate and there is no mention of its widespread use; in fact the history of the epidemic itself shows the lack of effective control.

The clinical features were varied and every organic system was affected. Headache was always violent, and accompanied by bilious vomiting and pain in the joints. There was usually only one relapse, which ensued after a week's apyrexia. The most frequent complications were hepato-nephritis and peripheral haemorrhages. Neurological forms occurred, especially pseudo-meningeal conditions and various psychoses. Ophthalmic complications were numerous; some of these were associated with the arsenic therapy. Premature termination of pregnancy was virtually inevitable, and this is ascribed to the death of the ovum after an enormous drop in the proteins in the maternal blood, which leads to dehydration and cachexia.

Mortality figures cannot be assessed accurately, but apparently varied in hospital cases from 3·6 per cent. in the well-to-do, to 8·7 per cent. in the poverty stricken. In the untreated, the figure varied between 5 and 10 per cent.

Different spirochaeticidal drugs were employed; antimony, bismuth and mercury salts were relatively inefficacious. Pentavalent arsenic was successful in curing the infection, but was sometimes followed by ocular disasters. The best drugs were the less toxic trivalent compounds (Neoarsphenamine, Mapharsen). The standard course of the former was 0·3 gm. the first day, 0·45 gm. the second and 0·6 gm. the fourth. An interesting new method was employed on 32 cases, namely, treatment with convalescent serum (20 cc. intravenously); 80 per cent. of the patients so treated were cured in 12 hours.

The authors conclude by stating that the immense region along the South Coast of the Mediterranean is the real sanitary frontier of Europe, a frontier easily crossed because the Mediterranean is a sea which unites rather than divides; beyond this frontier all the major epidemic diseases are rampant.

P. C. C. Garnham

GAUD, M., KHALIL Bey, M. & VAUCEL, M. **The Evolution of the Epidemic of Relapsing Fever, 1942–1946.** *Bull. World Health Organization* (United Nations). 1947/48, v. 1, No. 1, 93–101.

This paper forms a corollary to the one abstracted above (GAUD & MORGAN) and describes the extension of the epidemic throughout North Africa and the Middle East. The chronology of the disease in the larger foci appeared to be as follows:—

Last quarter of 1942	...	Fezzan, S. Tripolitania
October 1943	...	Tunisia
November 1944	...	Algeria
Early 1945	...	Morocco
November 1945	...	Tangier
1945	...	Egypt
1945	...	Kenya
February to June 1945	...	Iran

The epidemic traversed the whole of North-West Africa like a storm. Eastwards, the disease was first recognized at Assiut in October, 1944, but this threat to Egypt did not materialize until the following year, during which and in the first half of 1946, over 100,000 cases were reported, the peak notifications being in April, 1946. Throughout 1945 and 1946, small numbers of cases occurred in the Middle East, including Transjordan, Palestine, Syria, Irak and Aden. The disease attained epidemic proportions in Kenya and Iran.

The threat to French West Africa was partly averted by the institution of strict sanitary measures at Dakar on the arrival of convoys, but there is nothing to prevent the importation of the disease by land and the danger to this territory remains great.

Relapsing fever in epidemic form in Europe was confined to Rumania, where over 5,000 cases occurred in the first six months of 1946. It is unknown whether there is an aetiological connexion between this focus and the outbreak in North Africa.

The epidemic started as a few cases in a semi-desert region, progressively invaded the whole of North Africa from the Atlantic to the Red Sea, and is now threatening Central Africa and Europe.

P. C. C. Garnham

SALLE, L. La fièvre récurrente à Fès (1945–1946). [**Relapsing Fever in Fez.**] *Cahiers Méd. Union Française.* Algiers. 1947, June, v. 2, No. 11, 431–7.

The author states that the infection seems to have been brought into Fez by agricultural workers from the Oujda, early in May, 1945. The number of

cases reached a maximum in September, since when it has persisted at a somewhat lower level. Lice, and "probably" bugs, are considered to be the carriers. [There is no evidence in support of this statement.] The author observed and treated more than 1,000 cases during eight months ending January, 1946.

The incubation is said to be very short, only 2 or 3 days, and the author states that he was bitten by a louse on Wednesday at 8 p.m., and developed a febrile attack on Saturday at 2 p.m. A few observations are given on the clinical symptoms of the patients. The treatment adopted was acetylarsan, during the first 48 hours, and Mapharsen or Fontarsan when the infection was at its height. *E. Hindle*

BODMAN, R. I. & STEWART, I. S. **Louse-borne Relapsing Fever in Persia.** *Brit. Med. J.* 1948, Feb. 14, 291–3, 2 charts. [14 refs.]

Between November, 1945, and June, 1946, an epidemic of louse-borne relapsing fever occurred in Abadan, 1,087 cases being admitted to the isolation hospital. The authors have found no report in the literature of louse-borne relapsing fever in Persia, but the present epidemic was undoubtedly part of the widespread epidemics in the Mediterranean and North Africa during 1943–45. The epidemic closely followed the cold weather, and quickly declined as the general temperature began to rise: charts comparing this outbreak with a typhus epidemic in Abadan in 1943 show a striking similarity in the critical temperatures for the termination of the epidemics.

The diagnosis of louse-borne infection was based on the following points: (1) No tick focus has been found in Abadan and it is believed that no human ticks occur there. (2) Lice were found to have infested 88 per cent. of the patients admitted to the isolation hospital. (3) *Trep. recurrentis* was found in lice taken from the patients. (4) The epidemiological features were characteristic. (5) Mass disinfestation with DDT powder caused a drop in the weekly admissions.

Special clinical examinations were made of the last 214 cases admitted. Most of these patients were young adult males of the labouring and unemployed classes. The symptomatology is described. A point of interest was the frequency with which patients could fix the time of onset, which was ushered in with a splitting frontal headache. The period of apyrexia lasted about 9 days, although the most constant time-relationship was from onset to relapse, which averaged 14 days. Rashes were rarely seen; in those few patients having a petechial rash on the trunk, the Weil-Felix reaction showed only a slight *Proteus OXK* agglutination (*e.g.*, 1/25+, 1/50±). Jaundice was not uncommon: in 9 cases it was marked, and this was a bad prognostic sign—two of such patients died. The spleen showed all degrees of enlargement. The percentage incidence of symptoms and of signs is shown in tabular form and the authors note that the central nervous system is predominantly affected: 90 per cent. of their patients complained of headache and 77 per cent. of backache in the thoracic and upper lumbar regions. Two patients had mental derangement and there was one case of transverse myelitis. These last three were however the only complications seen in the central nervous system. Respiratory complications were the commonest, amounting to 60 per cent.: they varied from "cough" to bronchopneumonia. The overall death rate amounted to 1·11 per cent.

The 214 cases specially studied were treated in two groups. Group I (97 patients) were given 0·45 gm. NAB intravenously on admission: 11 patients relapsed once. In group II (117 cases) the dose was not given until the case

relapsed, which occurred in 75 cases. This saved the drug, which was short at the time, and also demonstrated its effectiveness in group I.

Few reactions followed the injection of NAB : no definite time interval was noticed between the injection and the crisis.

Of the nine patients with marked jaundice, three were not given NAB on admission owing to the liver damage already present : two of these three died. The remaining six received NAB on admission and none of them died.

H. J. O'D. Burke-Gaffney

BALTAZARD, M., BAHMANYAR, M. & MOFIDI, C. Fièvres récurrentes transmises à la fois par ornithodores et par poux. [**Relapsing Fevers transmitted both by *Ornithodorus* and Lice.**] *Ann. Inst. Pasteur.* 1947, Nov., v. 73, No. 11, 1066–71.

The authors have shown the resemblance between *Spirochaeta recurrentis* and certain strains of spirochaetes occurring in rodents and *Ornithodorus* [see this *Bulletin*, 1947, v. 44, 906].

In a first series of experiments, various batches of *Ornithodorus erraticus*, *O. lahorensis*, *O. turicata* and *O. parkeri* were fed on newly born rabbits heavily infected with *S. recurrentis*, and subsequently tested for infectivity, with uniformly negative results.

In a second series, human lice were fed on newly born rabbits infected respectively with a strain of *S. microti* from *O. erraticus* obtained in Persia, and *S. turicatae* and *S. hermsi*, both North American strains isolated from *O. turicata* and *O. hermsi* respectively. The lice were fed once on a heavily infected rabbit and subsequently maintained on a human subject. After intervals ranging from 9 to 12 days the lice were ground up and inoculated into newly born rabbits. In every case these became infected, showing that these naturally occurring rodent strains, although normally transmitted only by ticks belonging to the genus *Ornithodorus*, are also capable of survival in the human body louse.

E. Hindle

WOLSTENHOLME, B. & GEAR, J. H. S. **A Complement Fixation Test for the Diagnosis of Relapsing Fever.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 513–17.

It is notoriously difficult to find *Trep. duttoni* in many chronic infections of relapsing fever during the apyrexial intervals. The authors have therefore devised a complement fixation test as an additional diagnostic aid.

The antigen is prepared by establishing *Trep. duttoni* in egg-culture. This is achieved by inoculating eight fertile eggs on the 7th day of incubation, through the blunt air sac end, with 0·4 cc. of heart blood from an experimentally infected mouse. After a week's incubation at 37°C., the eggs are opened, and the blood-vessels of the chorio-allantoic membrane are torn and allowed to bleed into the allantoic fluid : this mixture serves as an inoculum (0·1 cc.) for further batches of eggs the strain from which, in the authors' case, has been subcultured for ten weekly passages with somewhat variable growth of spirochaetes.

A sample of the blood-allantoic-fluid mixture is examined by dark ground and stained smears, and it is only used if the degree of infection is profuse, *e.g.* 50 to 100 spirochaetes per field. The harvested fluid is centrifuged at 1,000 r.p.m. for 5 minutes, and the supernatant then centrifuged for 3 hours at 2,000 r.p.m. The resulting white sediment represents the spirochaetes, and the supernatant allantoic fluid is now replaced with 0·3 per cent. sterile phenol-saline. When this is shaken, an even suspension is obtained and this constitutes antigen :

its anti-complementary properties were found to be low and it could be used undiluted. [For detailed steps in the egg-culture and preparation of the antigen, the original paper should be consulted.]

For the test, the sera were inactivated at 56°C. for 30 minutes and serial dilutions were made from 1/12·5 to 1/100 and thereafter to 1/3,200.

Tubes corresponding to each dilution were set up and to each was added 0·1 cc. of the appropriate serum dilution and 0·1 cc. each of 3 M.H.D. guinea-pig complement and of undiluted antigen. One extra tube was used as an anti-complementary control and contained 0·1 cc. of normal saline instead of antigen. The tubes were placed in a 37°C. water bath for one hour, when fixation took place. To each tube, 0·1 cc. of 3 per cent. washed sheep cells, sensitized with 6 M.H.D. of amboceptor, was added and the tubes were incubated at 37°C. for a further 30 minutes, after which the results were read.

A table shows the results of the test in 6 confirmed cases of relapsing fever. All gave a positive result in a titre of 1/25 and five of the six were + or ± at 1/100.

Twenty-four sera sent for routine blood grouping were negative; of thirty sera giving a strongly positive Wassermann reaction, one was anti-complementary in the present test, 4 gave a ± result at 1/12·5 and the remaining 25 were negative. Seven sera from patients suffering from typhus, rheumatic fever, malaria, virus pneumonia and tuberculosis were negative, with the exception of one serum from a case of typhus fever which was positive at 1/12·5. All these tests were adequately controlled.

The authors conclude tentatively that fixation of complement in a titre of 1/25 and over should be taken as " diagnostic " of relapsing fever.

The time of development of the specific antibodies and the period of their persistence after apparent cure will be investigated: but in one case it was shown that these antibodies were present in low, though provisionally diagnostic, titre at the end of the first bout of fever. A point of interest is that in four of the six known cases of relapsing fever, blood films were negative for spirochaetes at the time the blood was taken for the complement fixation test.

The authors suggest that this complement fixation test promises to be of value in cases where finding the spirochaete in the blood is unlikely: in surveys of the incidence of relapsing fever; and possibly as a test of cure, though this aspect has not yet been studied. *H. J. O'D. Burke-Gaffney*

DEANE, Maria P. Verificação da infecção natural de ratos por Leptospira icterohaemorrhagiae na cidade de Belém, Pará. [**Natural Infection of Rats with** *Leptospira icterohaemorrhagiae* **in the City of Belém, Pará.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, July, v. 1, No. 2, 261–71. English summary.

In Belém, northern Brazil, the author found a natural infection with *Leptospira icterohaemorrhagiae* in 4 of 15 *Rattus norvegicus*, 4 of 19 *R. rattus* and 3 of 22 *R. alexandrinus*.

Infection was detected by dark-ground examination either of urine or of kidney suspension or both, and by animal inoculation. Eight strains were highly virulent for white mice. Of 104 white mice inoculated with infected material, 28 died of causes other than leptospirosis: the remainder were jaundiced and usually showed pulmonary haemorrhages at postmortem. A few mice without jaundice recovered and later showed leptospirae in the urine: two of them were still passing these organisms in the urine after 3 months' observation. Young white mice (3–4 weeks) proved very susceptible as laboratory animals.

Strains from wild rats were grown on Vervoot's medium and 25 per cent. rabbit serum in the medium, instead of 0·5 per cent., provided the best results.

A strain which proved infective to chick embryo appeared to take on increased virulence since, after passage, it killed 3 mice in 4 to 5 days, although previously it had killed mice in 10 to 14 days.

No human cases of Weil's disease have been recognized in the Amazon region so far: but in view of the comparatively high infection rate in rats in Belém and the potential opportunities for human infection, it is important that medical practitioners should have the possibility constantly in mind.

H. J. O'D. Burke-Gaffney

LEPROSY

INTERNAT. J. LEPROSY. Cleveland, Ohio. 1944, Dec., Suppl. to v. 12, 65 pp. **World Wide Distribution and Prevalence of Leprosy.**

CONTRERAS DUENAS, F. **Leprosy in Spain.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 178–82.

DE SOUZA-ARAUJO, H. C. La lèpre en Scandinavie. [**Leprosy in Scandinavia.**] *Bruxelles-Méd.* 1947, Dec. 21, v. 27, No. 51, 2809–10.

DUBOIS, A. La lèpre au Congo Belge en 1938. (D'après les rapports et documents de L. VAN HOOF, Médecin en Chef de la Colonie, et de nombreux médecins et missionnaires de l'assistance médicale indigène.) [**Leprosy in the Belgian Congo.**] *Institut Royal Colonial Belge. Section des Sciences Naturelles et Médicales. Mémoires.* (Collection in–8°.) 1940, v. 10, No. 2, 60 pp., 1 map. [Bibliography.]

This report gives a valuable summary of the measures for long in use in the Belgian Congo for the control of leprosy, and is based on reports by many medical workers, which should be read by leprologists, especially those engaged in similar work in backward tropical areas.

Agricultural colonies for leprosy patients have been instituted in this territory since 1927, mainly under the care of medical missionaries. Since 1937 a Commission has collected information on the endemicity of the disease, which was condensed in a report by Dr. VAN HOOF, the chief medical officer, on which the present publication is based. The geographical distribution of leprosy is first dealt with; at the end of 1938, the known cases were estimated at 60,000, or a mean of about 0·55 per cent. of the population. This is considered to be a maximum figure, as other skin diseases are sometimes erroneously diagnosed as leprosy. Tables at the end of the report show 18,658 as segregated, including many patients with neural disease. It is not possible to say if the incidence is increasing or not. The north shows higher rates than the south. Another table shows 64,554 under treatment. The number of children infected is low except in highly infected areas, and females suffer nearly as much as males. The proportion of lepromatous cases is only 10 to 15 per cent. of the whole; the disease is therefore of a mild type in this region though advanced mutilated cases are seen. It is not held that the nerve type is completely non-infective, though the main sources of infection are the lepromatous cases.

The report goes on to deal with local variations in incidence, and records a detailed survey of three highly infected villages with up to 10 per cent. of their occupants infected; the interesting suggestion is made that it would be simpler

in their case to remove the healthy than to isolate all the infected elsewhere. The great difficulties in dealing with a highly infected area of very poor and backward people living in a high degree of general and sexual promiscuity is well brought out. The commonest exposure to infection is domestic. Some differences of opinion are quoted regarding the effectiveness of chaulmoogra preparations and some doctors advocate their intravenous use.

Lastly, prophylactic measures are dealt with and preference is given to agricultural colonies containing about 300 persons frequently visited by a European doctor. At present these colonies contain a large proportion of neural cases, but the question of isolating only the more infective lepromatous patients is under consideration. A Government circular of 1937 on the campaign against leprosy is reprinted in this interesting publication.

L. Rogers

LARA, C. B. **The further Role of the Culion Leper Colony.** *J. Philippine Med. Ass.* 1947, Oct., v. 23, No. 10, 465–71.

YBARRA PÉREZ, R. & GONZÁLEZ PRENDES, M. A. La lepra y el estado civil de los enfermos de lepra en Cuba. [**The Civil State of Leprosy Patients in Cuba.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1947, Apr., v. 4, No. 2, 72–6.

The author gives figures which indicate that the percentage of married persons suffering from leprosy among the sick population in Cuba is 15·67 per cent. higher than that of the married persons in the whole of the healthy population of that country ; but the percentage of those in hospital is less than that of the ambulatory cases, owing to a number of social conditions.

On the other hand, the percentage of unmarried persons with leprosy among the sick population is 16·58 per cent. less than that of the unmarried in the whole population ; and the percentage of ambulatory cases is less than that of the unmarried hospital patients.

The social causes and significance of these findings are discussed.

H. J. O'D. Burke-Gaffney

FLOCH, H. **On the Epidemiology of Leprosy in French Guiana.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 183–8.

This is an instructive account of a careful inquiry on modern lines. In the course of 21 years, 1,447 cases of leprosy were registered, of whom 1,131 remain, or 5·1 per cent. of the population, a lower figure than earlier estimates. Altogether, 253 occurred among the penal population, 157 of whom were Europeans. Early cases have been sought for, and the unregistered cases are estimated not to exceed 300, bringing the total incidence to 6·5 per cent. There were 710 males and 478 females. Children up to 15 years of age formed 43·8 per cent., and persons over 25 years formed only 37·7 per cent. of the whole. Examinations of school children showed that 49 per cent. of new cases occurred in children up to 15 years of age. Contagion among school children is real and the results of segregating all those discovered resulted in a progressive diminution of new cases in the schools, from 26 in 1939 to only 8 in 1945. The disease is not hereditary, and familial infection is a proven fact. A servant had apparently infected five infants under her care. A table indicates transmission to collateral more often than to direct descendants. In children, the maculo-anaesthetic form is most frequent, and it is considered to be the least dangerous. On the other hand, Europeans are usually only infected after long residence and with a longer incubation period than in the case of indigenous

children, who appear to be more susceptible. The proportion of progressive and serious types is greater in Europeans, who appear to have less resisting power than the indigenous people ; this indicates the presence of a relative immunity among the Creole population, who have long been exposed to infection. Mitsuda reactions were positive in 90 per cent. of tuberculoid, 51 per cent. of neural, 1 in 12 of mixed cases, and were negative in all lepromatous ones. In healthy children under 10 years old, no positive reactions were met. An attempt to immunize children by inducing positive reactions is suggested.

L. Rogers

RISI, J. B. **Frequency of the Clinical Types of Leprosy according to the Natural Regions of Brazil.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, July–Sept., v. 15, No. 3, 246–57.

Tables are given of the incidence per mille and the percentages of the different types of leprosy in relation to geographical and climatic conditions. The very hot humid Amazon river basin shows the highest rates of 1 to 3·8 per mille, but with fewer severe lepromatous cases. On the contrary, the dry north-east region has the lowest rates of 0·9 to 0·1 per mille, but with a larger proportion of lepromatous cases. The eastern, southern and west-central regions, with cooler climatic conditions, present intermediate data. The author agrees with Rogers that hot humid climates favour the spread of leprosy, and he thinks that they act by adversely affecting the body metabolism rather than by an indirect effect in favouring the transmission of the disease. [Rogers suggested that the innumerable insect bites of hot damp climates favour the entry of lepra bacilli from contact cases through the puncture or abrasion lesions of the skin.] The author also suggests that humidity favours a less severe evolution of the disease and that a cold climate favours more acute development.

L. Rogers

MENDES, P. & MANGEON, G. **Leprosy in the State of Rio Grande do Sul.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, July–Sept., v. 15, No. 3, 258–63.

DUBOIS, A. Classification de la lèpre. [**Classification of Leprosy.**] *Acta Tropica.* Basle. 1947, v. 4, No. 4, 289–97.

The author criticizes the classifications of South American workers and that of TISSEUIL as leaving many difficulties, especially for the clinician, in the neural cases. He suggests classification based on the amount of bacillary invasion of the tissues, as determined by simple routine examinations, rather than on less easily ascertained histological grounds, and suggests the following classification, in which the old symbols are shown after each form in brackets.

A.—Bacilli rare or absent. Subdivisions : A–M, flat macules. (Ns) : A–A, anaesthetic-acroteric. (Na) : A–M–A, maculoanaesthetic. (Ns–Na) : A–T, elevated macules, tuberculoid major. (NT) : A–t, elevated macules tuberculoid minor. (Nt) : A–T–A (or t–A), elevated macules with lesions of nerves (NT (t)–Na).

B.—Bacilli numerous (++ or +++) : B.M, Macular (Lm) : B.L, Lepromatous, nodular. (L.1.2.3.) : B.I, do. localized infiltration. (L.1.2.3.) : B.D, do. diffuse infiltration (Ld) : B.G, do. generalized : B.A, anaesthetic-acroteric. (LN) : A″, anaesthetic-acroteric (secondary).

L. Rogers

PORTUGAL, H. **Contribution to the Study of the Classification of Leprosy: Aspect of Lesions, Antigenic Response, and Presence of Micro-Organisms in Histologic Structure.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 162–8.

In this paper, the practical application of the South American classification is considered in the light of histological examinations in 70 cases, in the majority of which an immediate diagnosis of type was possible. In others, time was required to watch the evolution. Among 13 lepromatous cases, mostly fairly early ones, all were positive bacteriologically and gave negative Mitsuda reactions. Moreover, the lipid staining test was positive except in very early cases. The tuberculoid group included reacting and quiescent cases. One reacting case developed into the lepromatous type during eighteen months; a second remained tuberculoid and in a third the evolution remained doubtful. Among 32 quiescent cases, the majority being of one to six months' duration, all were uniformly tuberculoid and negative bacteriologically to routine examination and all but two were positive to the Mitsuda test. The "uncharacteristic" type numbered 18; they mostly showed achromic or hypochromic spots or merely anaesthetic areas. Only two showed bacteria and half were Mitsuda positive and half negative. In all, only small lymphocytic infiltration was found around the small vessels. In two cases, tuberculoid structure developed later. Re-examinations were not done in a number of these cases, so their evolution is uncertain and no one can foretell their outcome. They may remain "uncharacteristic" or may evolve into tuberculoid or lepromatous cases.

L. Rogers

RODRIGUEZ, J. N. **Observations on the Classification of Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, July–Sept., v. 15, No. 3, 274–302. [52 refs.]

This is a full discussion of this difficult subject which should be read by all leprologists. The author first traces the evolution of classification from the old Norwegian one of "nodular" and "anaesthetic" up to the recognition of a third or "tuberculoid" type by the Cairo Congress in 1938, based on histology largely due to the work of WADE. This was soon recognized to be still inadequate, especially by South American pathologists, which led to the adoption, by the Second Pan-American Conference at Rio de Janeiro in 1947, of the following types.

Uncharacteristic (I) or Unidentified; Macular, Neural or Neuro-Macular.
Lepromatous (L); Macular, Infiltrative, Nodular, Neural and Generalized.
Tuberculoid (T); Macular, Papular, Neural and Reactive.

It differs from an earlier South American classification in raising the "uncharacteristic" form to the status of a fundamental type. Its scientific basis is histological, for the uncharacteristic type is characterized by the presence of only simple round-cell infiltration, as opposed to the tuberculoid granuloma and foamy-cell infiltration respectively of the other types.

The present author proposes to add a fourth type, characterized by only interstitial proliferation as found in the maculo-anaesthetic (neuro-leprid) and he calls the second type with round-cell infiltration simple macular (leprid). He further discusses the question of the evolution of tuberculoid into lepromatous disease and accepts the evidence of South American workers, who followed the change of typical Mitsuda- or lepromin-positive tuberculoid cases into negative reacting lepromatous cases as proof of such a change, although it usually takes a long time to be brought about. He also discusses the difficulty in classifying the common "neural" cases which require further biopsy studies. He suggests that the lepromatous form is the characteristic fully

developed leprosy in non-resisting patients; and the other three types are either benign atypical cases or evolutionary forms of the earliest stage of the disease. The histological classification cannot be adopted by the great majority of those working in the field at the control and treatment of the disease for want of time and opportunities for making biopsies. He therefore proposes the following sub-divisions of the four fundamental types :—

1. *Interstitial.* MA_1 (Mitsuda positive or negative): MA_2 (moderate atrophies, Mitsuda positive); and MA_3 (marked atrophies, paralyses, trophic ulcers. Mitsuda strongly positive).

2. *Perivascular Round-Cell.* (Uncharacteristic stage.) Mitsuda plus or minus: RCpt, pre-tuberculoid (leprid), RCpl, pre-lepromatous; RCr, residual.

3. *Tuberculoid Stage* (T). (Mitsuda positive): T, simple (torpid or minor); Tm, macular; Tmp, maculo-papular or papular; Tmn or Tmpn, with nerve involvement; TR, reacting tuberculoid (major); TRn, with nerve involvement; Tr, residual; Tlaz, lazarine leprosy (hyperergic).

4. *Lepromatous* (foamy cell) type (Mitsuda negative), C_1, C_2, C_3 with or without N_1, N_2, or N_3.

For further detailed description of the above forms, the original paper must be consulted. A good bibliography is appended. *L. Rogers*

DE SOUZA LIMA, M., BARBA RUBIO, J., DE SOUZA LIMA, L. & RATH DE SOUZA, P. **Pathogenic Bases of the South American Classification of Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 169–74.

This paper deals with the pathogenesis of leprosy in relation to immunology, and the histopathological structure of the lesions, with a view to explaining the mutations from one type to another which occasionally occur. *Myco. leprae,* on entering the human host can survive for long in the interstitial connective tissue without multiplying actively, until it succeeds in penetrating into living cells. The bacilli are then phagocytosed by macrophages and histiocytes, which may react by destroying the bacilli by lysis in resistant tuberculoid forms; or the bacilli actively multiply in the cells to form the typical foamy cells seen in lepromatous cases with little resistance to the invasion. When the body cells remain indifferent and non-reactive the "uncharacteristic" type results for a time. The two types of reaction may occasionally occur in the same lesions as a "transitional" form of an unstable nature, the ultimate development of which is doubtful. In such, the action of drugs or other favourable influence may produce a structural change from lepromatous to the tuberculoid type. The South American classification is based on clinical, immunological and histological grounds. *L. Rogers*

AZULAY, R. D. **The Mitsuda Test in Non-Leprous Persons in a Non-Endemic Country.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, July–Sept., v. 15, No. 3, 264–6.

"1. Among 73 American adults of both sexes, but predominantly Negroes, 74 per cent reacted positively to full strength lepromin, but only 33 per cent. to a 1 : 10 dilution of the same lepromin.

"2. Among males, 66 per cent. reacted positively and among females 86 per cent.

"3. Concentration of bacilli in the antigen is important and should be standardized if results are to be compared.

"4. The authors believe that the mechanism of the Mitsuda phenomenon is due to a basic constitutional reactivity of the tissues. This natural tissue response may be accelerated either by *M. leprae* or *M. tuberculosis.*"

PORRITT, R. J. & OLSEN, R. E. **Two Simultaneous Cases of Leprosy developing in Tattoos.** *Amer. J. Path.* 1947, Sept., v. 23, No. 5, 805–17, 8 figs. on 3 pls. [10 refs.]

This is an important contribution to the disputed question as to the inoculability of leprosy. The authors quote the opinion of JEANSELME that there is no adequate proof of the transmission of leprosy by inoculation, and also cites cases reported by ROGERS and MUIR to the contrary effect. They now record the cases of two men of the U.S.A. Marine Corps, who were tattooed successively by the same man on the same day in June 1943, at a time when both the soldiers and the tattooer were drunk. Two and a half years later, in 1946, both men developed discoloured anaesthetic patches around the new tattoo marks, but an earlier tattoo mark in one was not involved. Portions of the lesions were removed for examination in both men without any discomfort in spite of the fact that no anaesthetic was used. Guineapigs were inoculated, with negative results as regards tuberculosis. Sections of the tissues of both showed typical tuberculoid changes; scattered acid-fast bacilli were readily found in one and less frequently in the other. The second patient developed similar patches on his other arm subsequently to those at the site of the tattoo mark. Sections of both were sent to the Carville Leprosarium, the authorities of which came to an unequivocal diagnosis of "typical tuberculoid leprosy". Both the naked-eye and the microscopical characters of the lesions are illustrated by plates.

The authors conclude that: "These two cases provide strong evidence for the spread of leprosy by inoculation." *L. Rogers*

SCHUJMAN, S. **Therapeutic Value of Chaulmoogra in the Treatment of Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 135–45, 6 figs. on 2 pls.

The author stresses the necessity of early treatment of lepromatous patients by large doses of chaulmoogra oil regularly continued until the patients have remained free from symptoms for some time. He writes from seventeen years' experience and deals only with lepromatous cases, because other forms may recover spontaneously. He thinks reported failures are due to deficient doses and duration of the treatment. He finds that untreated lepromatous cases always become worse and those treated irregularly show an unfavourable evolution; but previously untreated cases nearly always improve, often rapidly, although renewed treatment after an interval is less certain and slower. Cases not benefited by small doses are benefited by larger ones and may become bacteriologically negative. The proper method is to inject the maximum amount which can be tolerated in the minimum time. All hospital patients who became clinically and bacteriologically negative had received a total dosage of 1,500 cc. of ethyl esters, preferably with 4 per cent. creosote; but of those showing only slight improvement, only 27 per cent. had received the full dosage. The injections are made intramuscularly and intradermally. With the full dosage, 40 per cent. of all treated lepromatous cases have been rendered clinically and bacteriologically negative, and 40 per cent. have become definitely, and not only slightly, improved with the injection of a total amount of 30 cc. weekly. The author is of the opinion that over 80 per cent. of failures in lepromatous cases are due to deficient dosage and irregular treatment. The few failures are nearly all very advanced cases. Illustrative photographs of patients before and after treatment confirm the author's claims. *L. Rogers*

DE SOUZA-ARAUJO, H. C. Le Promin dans le traitement de la lèpre. [**Promin in the Treatment of Leprosy.**] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 195–200.

FLOCH, H. & CAMAIN, R. Sur le traitement de la lèpre par la Promin, en Guyane Française. [**The Treatment of Leprosy with Promin in French Guiana.**] *Institut Pasteur de la Guyane et du Territoire de l'Inini. Publication No. 160.* 1947, Aug., 8 pp.

ROSS, Hilary. **Blood and Urine Concentration of Promin, Diasone, and Promizole in the Treatment of Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, July–Sept., v. 15, No. 3, 236–45, 2 figs.

WHARTON, L. H. **Preliminary Report on a New Sulphone Drug "Sulphetrone".** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, July–Sept., v. 15, No. 3, 231–5.

"Sulphetrone in 3·0 Gm. daily dose, giving 1 tablet (0·5 Gm.) every four hours, has proved to be safe. We have seen only very mild toxic effects from the drug, nausea, which was quickly relieved by administering sodium bicarbonate, 30 gr. three times a day orally. There has been marked improvement in clinical symptoms, with flattening out of nodules. Bacteriological smears from nose and skin have shown marked improvement from month to month and one patient with positive nose and skin smears became bacteriologically negative in the fifth month.

"It should be noted that this trial was made on early L_1 cases that were free from any complications of the disease. Clinical trials continue and will be extended to include patients with more advanced lesions, and with complications."

FAGET, G. H. & ERICKSON, P. T. **Use of Streptomycin in the Treatment of Leprosy. A Preliminary Report.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 146–53.

The antibacterial action of streptomycin against the tubercle bacillus led to this trial. In 1945, the receipt of 50 million units allowed of only one patient being treated; the results were encouraging, but not definite, after several months. In June, 1946, sufficient streptomycin to treat 10 cases was received and ¼ gm. or 250,000 "s" units were injected every three hours for four months in 8 of the patients. Unpleasant, and even serious, toxic effects were observed, the most frequent being vertigo, with lasting deafness in one, eosinophilia, anaemia, loss of weight and low blood pressure, fever, headache, and casts and blood cells in the urine due to renal irritations. The drug requires further purification. Improvement was noted, but was not greater than that achieved with less toxic sulphones. It is too soon to judge of the value of streptomycin treatment.

L. Rogers

FITE, G. L., ERICKSON, P. T., GEMAR, F. & JOHANSEN, F. A. **Local Treatment of Leprous Ulcers with Crude Preparations of Streptomycin.** *Internat. J. Leprosy.* Cleveland, Ohio. 1947, Apr.–June, v. 15, No. 2, 154–61, 1 text fig. & 12 figs. on 3 pls.

Crude filtrates of *Streptomyces griseus* of local manufacture have been tested on leprous ulcers with promising results. The original paper should be consulted by those interested in the method of culture. The filtrate contained 28 to 40 microgrammes of streptomycin per cc. and was used by soaking layers of gauze with it and applying them to the ulcers with a protecting layer of rubber to prevent excessive drying. The gauze is soaked every twelve hours for a week and then renewed weekly until the ulcer is healed, provided that no irritation is produced. If erythema with vesiculation is produced, the filtrate

should be diluted 1 in 5 with boric acid. Thirty-six patients have been treated and in only one did toxic symptoms necessitate stopping the applications, and another patient objected to the bandaging. Notes of illustrative cases are given. They are divided into three groups. In group I, consisting of perforating ulcers of the sole of the foot, success was obtained in 18 out of 19; in mixed cases, in 11 of 14, and in the only lepromatous case treated. Sloughing varieties show most resistance to the treatment and complete healing was only obtained within two months in 45 per cent. Trophic ulcers respond best. Of the total cases, one-fourth healed in less than one month and 70 per cent. in two months. The results are therefore satisfactory. Photographs of cases before and after treatment are recorded. *L. Rogers*

HELMINTHIASIS

FEROLA, R. Sulla frequenza della parassitosi intestinale nell'infanzia. [**The Incidence of Intestinal Parasites in Children.**] *Pediatria.* 1946, July–Sept., v. 54, Nos. 7/9, 426–31. [11 refs.] English summary (6 lines).

A survey of 244 children in Naples.

BASSÈRES, M. S. & PANTOJA, W. P. Verminoses—Algumas considerações em tôrno das verminoses na área do Rio Dôce. [**Observations on Worm Infestations in the Rio Dôce Area, Brazil.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, July, v. 1, No. 2, 235–49, 1 map & 4 figs. English summary.

CAUSEY, O. R., COSTA, O. & CAUSEY, C. E. Incidência de parasitos intestinais do homem em Belém, Pará e visinhanças. [**Incidence of Intestinal Parasites in Man in Belem, Para and its Environs.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, July, v. 1, No. 2, 221–33, 5 figs. English summary.

DA COSTA, O. R. Incidência de parasitos intestinais em quatro cidades da Amazônia. [**Incidence of Intestinal Parasites in Four Cities of Amazonia.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, July, v. 1, No. 2, 203–19, 5 figs. English summary.

WILKINS, A. J. W. **Schistosomiasis in Salisbury, S. Rhodesia.** *Pub. Health.* Johannesburg. 1947, Nov., v. 11, No. 11, 4–6, 9–10.

This paper was read to a Health Officials' Congress in Southern Rhodesia by the M.O.H. of the capital city, Salisbury.

He gives figures from the health department files concerning African patients, showing that on single microscopic examinations 30 per cent. of 13,000 urines and 8 per cent. of 9,400 stools were positive for bilharzia eggs. He believes [probably rightly] that the true infection rate is much higher than this and goes on to discuss measures for its amelioration. Like most workers with primitive peoples, he despairs of an immediate public response to the provision of sanitary facilities, although he notes that in Salisbury, where numerous conveniences have been provided, there has been a considerable reduction in promiscuous fouling. He also feels that the numbers requiring treatment are too great for his department to be able to rely on mass treatment of infected people as a control measure. He has therefore set out to kill the bilharzial snails [he names

Physopsis globosa, but it is not certain whether this species or *P. africana* is more important] in the water around Salisbury, and he reports success with a copper-sulphate-bag method, as follows :—

"The salt, of which the larger lumps have been broken, is placed in a small bag of cloth mosquito netting, cheese cloth or organdie, which is attached by string or wire to a stick. The bag is then dipped in and out of the water along the sides of the pool or stream, particular attention being given to water in the vicinity of reeds or other grasses. In our experience it has been found that by moving along the bank fast enough to allow the bag to be submerged in the water and withdrawn immediately, and for this to be repeated at approximately 12- to 18-inch intervals when the flow is not too rapid or very considerable in volume, the concentration obtained has proved sufficient to kill 100% of the snails present."

[It must, however, be pointed out that this bag method is not of universal application. While no doubt satisfactory where river-banks are fairly level and well-defined, or in ditches or irrigation canals, it is of little value in the treatment of "wild" river-courses, with their broken and irregular banks. The author himself points out that the bag-method is being used in favourable conditions.]

He makes the interesting observation that it has been found possible to use his "anti-malarial gangs" on this snail destruction work, a great saving in expenditure.

His work shows that it is apparently possible to protect a small area in an infected country, when this is desirable because of the large concentration of people living in that area. *W. Alves*

ZITO, P. Tentativi di infestazione di molluschi nostrani con uova di *Schistosoma haematobium*. Osservazioni sulle uova ed azione di alcune sostanze su esse e sul miracidio. [**Observations on the Infestation of certain Molluscs with** *S. haematobium* : **the Effects of Different Substances on the Eggs and Miracidia.**] *Acta Med. Italica.* 1947, Dec., v. 2, No. 12, 375–7.

The English summary appended to the paper is as follows :—

"The author describes the characters of the molluscs, intermediate hosts of some trematodes which infest man : he reports on some negative attempts of infestation of molluscs (*Planorbis corneus*, *Phisa* [?*Physa*] *fontinalis*, *Heubania vermiculata*) with eggs of *Schistosoma haematobium* ; he exposes some observations on the eggs of *Schistosoma haematobium* and its miracidium, and on the action of some substances (eosin, trypaflavine, penicillin) on them ; eosin and trypaflavine kill the embryo : penicillin has no effect on the time of opening of the eggs and on the miracidium."

COWPER, S. G. **Observations on the Life-Cycle of** *Schistosoma mansoni* **in the Laboratory, with a Discussion on the Snail Vectors of** *S. mansoni* **and** *S. haematobium*. *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 173–7. [14 refs.]

The author, writing from the Liverpool School of Tropical Medicine, has succeeded in establishing a strain of *Schistosoma mansoni* in a monkey, after having infected a strain of *Planorbis boissyi* with miracidia obtained from infected faeces of patients who acquired the disease in Uganda. These snails were from an Egyptian stock, and the author also succeeded in infecting *Australorbis glabratus*, the tropical American intermediate host. He describes the technique adopted, which was perfectly simple.

The author also attempted to infect 22 specimens of an Egyptian strain of *Bulinus truncatus* with miracidia of *S. haematobium* from a patient who contracted the disease in Nigeria, but without success, though this species is well known as the intermediate host in Egypt.

In his discussion, the author notes that STUNKARD (unpublished note) failed to infect Egyptian *Planorbis boissyi* with Porto Rican *S. mansoni*. *Planorbis pfeifferi* is the chief host in West and Central Africa, and *Physopsis africana* has been claimed as a host by PORTER [see this *Bulletin*, 1920, v. 16, 131]. *Planorbis adowensis* is reported as a host in the French Sudan, and in North America a species of *Tropicorbis* has been experimentally infected.

For *S. haematobium* the normal intermediate host in West Africa is *Physopsis globosa*, and *Physopsis africana* in part of the Belgian Congo. In Mauritius *Bulinus forskali* is the host, but though this snail is common in Egypt and South Africa, it has not been incriminated there. *Bulinus truncatus* (of which *contortus*, *dybowski* and *innesi* are now regarded as synonyms) is the common host in Egypt. Other hosts of *S. haematobium* are *Planorbis dufourii* in Portugal and Morocco, though elsewhere *Planorbis* snails are not susceptible to *S. haematobium*; *Melanoides tuberculata* has been strongly suspected in the Sudan and Nyasaland [and *Limnaea natalensis* by PORTER (*ibid.*) in S. Africa; but see KERVRAN below.]

The author discusses this species-specificity, and even strain-specificity, and makes the point that it is obviously important in any "species sanitation" of snails. References are cited to the authorities for the statements made.

Charles Wilcocks

i. KERVRAN, P. Les hôtes intermédiaires des bilharzioses humaines à Bamako (Soudan français). [**The Intermediate Hosts of Human Schistosomiasis at Bamako, French Sudan.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 9/10, 349–52.

ii. ——. Contribution à l'étude de la faune malacologique du Soudan français. [**A Contribution to the Study of the Snails of the French Sudan.**] *Ibid.* 364–6.

i. The author recalls that SAUTET and MARNEFFE [this *Bulletin*, 1946, v. 43, 462] found that *Planorbis adowensis* Bourguignat, 1879 [=*Planorbis bridouxi*], was a natural host of *Schistosoma mansoni* near Bamako. He now records observations on other snails in the same area. No infection was found, nor could it be induced, in *Lymnaea natalensis* var. *undussumae* von Martens, with either *S. haematobium* or *S. mansoni*.

With *Physa tchadiensis* Germain, 2·5 per cent. of 788 emitted fork-tailed cercariae, and several which did not emit cercariae, during a month of observation became infected when exposed to *S. haematobium*, but not to *S. mansoni*. *Physa strigosa* von Martens [=*Physopsis africana*] was found infected in nature (26 per cent.), largely with *S. haematobium*, rarely with *S. mansoni*, as was proved by infection of rats. This snail is easily infected experimentally, and emits cercariae some 25 days later (*S. haematobium*) or 15 days later (*S. mansoni*) at 26°–28°C.

The author confirmed the work of Sautet and Marneffe with *P. adowensis*; 14·1 per cent. were infected in nature, and experimental infection was easily secured with *S. mansoni*.

ii. The author gives a list of fresh-water snails collected during an enquiry into the intermediate hosts of the schistosomes of man. Apart from the important snails mentioned in the previous abstract, he records shells of

Bulinus forskali (Ehrenberg), but has not found any living specimens. He also mentions a number of other snails which are not, so far as is known, concerned in human schistosomiasis. *Charles Wilcocks*

GIRGIS, B. & AZIZ, S. **Treatment of Schistosomiasis.** *Lancet.* 1948, Feb. 7, 206–9, 1 fig.

The authors have investigated the action of sodium antimony tartrate in the treatment of schistosomiasis, following the method of Alves and Blair with minor modifications.

The total dosage of (freshly prepared) sodium antimony tartrate was 1 grain for every 5 kgm. of body weight and was divided into six more or less equal doses, which were given on two successive days at 8 a.m., 11 a.m. and 2 p.m. Special precautions were taken to give the injection slowly. The drug was prepared in a solution of 1 grain in 1 cc., and out of 16 patients, 12 received the dose undiluted, but in 4 it was made up to 10 ml. with 5 per cent. glucose solution. All-glass " Record " and " Vim " syringes were employed.

The immediate reactions are described as rather severe and in some cases drastic, whether the drug was diluted or not. The commonest were cough, vomiting, tightness of the chest, pyrexia and pain in the arm or shoulder: sometimes pain in the joints, toothache, a metallic taste in the mouth, a sense of irritation in the bladder, or peculiar choreiform movements of the arms and legs. On the whole, the patients had no appetite and preferred to stay without food for the two days of treatment. They invariably looked ill and dreaded the injections. Out of 16 cases, 6 had a mild bradycardia after each injection. A minor drop in the systolic blood pressure was sometimes registered. Electrocardiographic records were made of every patient before treatment, at the end of the first and second day's treatment, and again within the following week. Changes in the QRS complex and T wave appeared at the end of the first day, becoming more pronounced as treatment proceeded. These changes were restored about the second day after treatment.

The haemoglobin percentage tended to rise during treatment and this was ascribed to haemoconcentration. All patients showed a loss of 1–3 kgm. in weight during the same period, but regained it within 10–14 days. In *S. haematobium* infections, the patients continued to show haematuria until the 10th day after treatment, but by the end of the second week all testified to the relief of urinary symptoms. On the second day after the end of treatment, all patients were still passing living ova; by the 23rd day any ova passed were dead, but in five instances they were passed continuously for eighty days. Observations on these ova appeared to indicate that, although temporarily damaged by antimony, some worms survive, and, after a period of cessation of oviposition, recommence reproduction. Dead ova are best demonstrated by sedimentation methods. In this state they are wrinkled, distorted and smaller than normal.

The difficulties of application of the two-day treatment in large-scale campaigns are obvious, therefore 9 patients were treated with the same doses spread over a six-day period.

On the whole, the reactions were fewer and milder. The urine was examined after the third injection, five days after the end of treatment and subsequently at weekly intervals. Three patients were passing ova on the 18th day and by the 53rd day living ova were detected in two.

The relapse rates in these two methods was 31 and 33 per cent. respectively.

While admitting that the two-day treatment of Alves is an advance over the original method, the authors consider it to be too drastic to be useful in large-scale campaigns. *P. Manson-Bahr*

NESS, A. T., BRADY, F. J., COWIE, D. B. & LAWTON, A. H. **Anomalous Distribution of Antimony in White Rats following the Administration of Tartar Emetic.** *J. Pharm. & Exper. Therap.* 1947, June, v. 90, No. 2, 174–80, 1 fig.

"Dogs and rats were injected with tartar emetic prepared from radioactive antimony. Antimony concentrations in the blood and tissues of rats were considerably different from those in dogs and, judged by available data, were also different from concentrations encountered in man, white mice, cotton rats, and hamsters.

"In white rats, the blood antimony is characterized by an increasing concentration beginning at 8 hours and lasting at least for 72 hours. This is in contrast to that in man and in the dog in which the concentration is decreasing to very low levels at these intervals.

"There is some indication that the antimony compound appearing in the blood of the white rat at later intervals is considerably less toxic to the rat than its tartar emetic precursor. It is suggested that results obtained in screening antimonial compounds in white rats be interpreted with caution until more is learned of the phenomenon."

LUTTERMOSER, G. W. **The Control of the Blood-Fluke Disease (Schistosomiasis) in Venezuela.** *Health & Sanitation Division Inst. Inter-American Affairs Newsletter.* Wash. 1947, Oct. (Schistosomiasis Number), 24 pp., 25 figs. & 3 maps.

This Newsletter is, no doubt, written largely for the non-medical reader, but its author is already well known for his work on the subject, and his description, based on his own experience, is comprehensive and most informative. The publication is a succinct account of control measures, and could hardly be bettered. Luttermoser himself has returned to the United States (he is a graduate of Johns Hopkins), but no doubt his methods will be continuously developed in Venezuela.

The area of schistosomiasis in Venezuela lies within a semicircle of 100 miles' radius, whose centre is at Catia La Mar; there are coastal foci and foci along the main drainage systems, and they involve a population of over one million. It has been estimated that there are more than 50,000 cases of schistosomiasis (*S. mansoni*) in the country. Diagnosis is made by faecal examination, by skin test with extract of adult *S. mansoni*, and at post mortem examination. (JAFFE at the Hospital Vargas had found it to be the cause of death in 5·4 per cent. of 2,461 autopsies, that it was present in 18 per cent., and that of those with the disease, 37 per cent. died of it.) Treatment is given to infected persons, at the various clinics, and tartar emetic and Fouadin are used.

Eradication of *Australorbis glabratus* (the snail host) includes the clearance of vegetation from irrigation canals, and the training or paving of the bed and banks of these canals, to increase the rate of flow. Water holes are filled in or drained, and copper sulphate or carbonate, or freshly-slaked lime, are applied where necessary. In some sections, irrigation ditches are placed in conduits where they run near houses, so as to protect them from fouling. Latrines are constructed and the people are educated in their use and instructed in the mode of infection. The disease is most prevalent among the poorer people, and it is thought that general education may be a potent force in reduction of infection.

An account is given of the various surveys made at Maracay, the El Valle river system and the Guarenas region. Snails occur in rivers where the current is slow and where there is much vegetation; optimum temperature is about 20°–26°C. Flooding may wash snails downstream into water holes or irrigation

canals. It was found (as had previously been known), that a standard sand filter will not hold back cercariae, but that standard chlorination of water, if carefully controlled, will destroy them.

Snails are found in great numbers in watercress gardens, sugar-cane plantations and other similar cultivated areas. Watercress cultivation is a most important industry ; the method adopted to eliminate the snails was to remove all vegetation from the beds (each about 12 square yards) and treat them with freshly slaked lime and dry them thoroughly in sunlight. The banks were built up and the irrigation inlets and outlets were strengthened. The snail eradication work was begun at the head waters and continued downstream, and the watercress gardens were mostly in the upper reaches. New plants were carefully washed in lime water before planting.

A reed is grown in these upper reaches, which is used for animal packs ; snail control in these gardens consisted largely of drying every 3 months, and applications of copper sulphate. Workmen are advised to wear rubber boots, and efficient latrines are provided.

The author thinks that control is possible by more extensive and intensive use of the measures discussed, but he places special emphasis on health education and sanitary improvement. *Charles Wilcocks*

REEVES, D. L. & KERR, R. W. **Schistosomiasis Japonica with Intracerebral Granuloma : Operative Removal with Recovery. Report of a Case.** *Arch. Neurol. & Psychiatry.* 1947, Aug., v. 58, No. 2, 207–20, 3 figs. [12 refs.]

In the literature on *Schistosoma japonicum* there are reports in only two cases of the successful surgical removal of intracranial granulomata attributable to this parasite. Both the patients made good clinical recoveries. A patient of the authors, a soldier of 29 when serving in the south-west Pacific area, developed diplopia, headache, and recurring convulsive seizures with loss of consciousness, in January 1945. In August 1945, a detailed physical examination revealed little more than bilateral papilloedema, slightly impaired stereognosis on the left side, and some weakness of the left hand grip. The cerebro-spinal fluid was at a pressure of 430 mm., but was otherwise normal. Subsequently ventriculographic study showed displacement of the ventricular system to the left, with similar displacement of the third ventricle. There was a noticeable filling defect in the posterior and temporal parts of the right lateral ventricle, which was flattened and depressed. A diagnosis of an intracranial expanding lesion in the right temporo-occipital area was reached, and as the patient had a history of a minor head injury in December 1944, the origin was considered to be a subdural haematoma.

Craniotomy was performed in the right occipito-parietal region. The dura was tense, and, on opening it, small whitish tubercles from a pin-point to a pin-head in size were seen on the surface of a tumour, which was indurated and rubbery. This was removed piecemeal and was found to contain small calcified areas. The tumour was about the size of an orange, and extended into the subtemporal area. It was thought to be an unusual type of glioma.

On pathological examination, many *S. japonicum* eggs were found in a granulomatous mass with large areas of caseous necrosis. There were scattered giant cells, and varying degrees of infiltration with eosinophils and with mononuclear phagocytic cells. Over the surface of the tumour there was thickening of the leptomeninges, with increased vascularity and some leucocytic infiltration.

On further questioning, in view of the pathological diagnosis, it was found that the patient had probably acquired his infection in Leyte in October or November 1944. Examination of the stools failed to reveal the presence of ova. He was treated with courses of stibophen and of antimony potassium tartrate,

and with potassium iodide by the mouth. The patient's recovery after the operation was uneventful, and in June 1946 he complained only of some general weakness and occasional headaches, particularly on the right side and at the back of the head.

The authors conclude with a brief historical review of the discovery of Asiatic schistosomiasis, and a consideration of its causation, symptomatology and treatment. They point out that their case presented none of the expected symptoms and signs of the disease, and so the correct diagnosis was not suspected until revealed by the pathologist. The importance of the condition is apparent in view of the large numbers of United States troops who served in the south-west Pacific and other endemic areas. *A. R. D. Adams*

VARTIAINEN, I. & BASTMAN-HEISKANEN, L. **On the Staining of Diphyllobothrium Ova.** *Ann. Med. Intern. Fenniae.* 1947, v. 36, No. 3, 729–39. [11 refs.]

" The ova of *Diphyllobothrium latum* behave differently in eosin solution. Some are stained red, while others remain colourless. This is true both of ova found in the excrements of worm carriers and of eggs taken from the tapeworm itself.

" The percentage of stained eggs is lowest in the first metres of the worm, but grows higher toward the end part of the parasite, and may then be as high as one hundred per cent. Correspondingly, the number of living larvae is highest in the first metres and very low in the last. The ability of staining undoubtedly means that the ovum is dead, and this may be regarded as indicating decreased vigour in that part of the parasite.

" In all, seventeen worms were examined in order to find out how far the ova were stainable in the different parts of the worm. In this respect, there were differences between the individual worms."

TOTTERMAN, G. **Is the Broad Tape-Worm the Causal Agent of Hypochromic Anemia ?** *Ann. Med. Intern. Fenniae.* 1947, v. 36, No. 1, 185–90. [13 refs.]

It is established, says the author, that *Diphyllobothrium latum* may cause typical pernicious anaemia in some of its carriers. In a far greater number, however, there is a " hyperchromic, or an almost normochromic mild anaemia " and these latter cases are cured by a vermifuge and should therefore be considered as being due to the tapeworm. Opinions vary about the relation between hypochromic anaemia and this tapeworm. The history of these questions is briefly discussed with references to the literature.

The author himself studied 43 cases, 34 females and 9 males, with hypochromic anaemia and *D. latum* ; most of them had other diseases as well. Thus, 23 had acute infections which included pneumonia, exudative pleurisy, pyelitis, acute polyarthritis and acute nephritis. Three patients had chronic infections and 2 had tumours. It is, the author says, " highly probable " that in these cases the complicating diseases and not the worm caused the hypochromic anaemia. But 10 patients had no complicating diseases. Nine of these had " anaemia achylia simplex " and one had chlorosis.

The author discusses these ; his general conclusion is that no single case of hypochromic anaemia in his series was definitely improved by a vermifuge

alone ; that the presence of *D. latum* does not seem to impede the spontaneous improvement of the blood picture after an infection or to check the effect of iron in a post-haemorrhagic or an essential hypochromic anaemia ; and that broad tapeworm anaemia and hypochromic anaemia are not causally connected. This is probably the reason why the combination of broad tapeworm and hypochromic anaemia is relatively infrequent, especially in comparison with the frequency of hyperchromic anaemia and broad tapeworm. [See also this *Bulletin*, 1948, v. 45, 97, 198, 260.] *G. Lapage*

HIRVONEN, M. **Observations throwing Light on the Pathogenesis of Pernicious Tapeworm Anaemia.** *Ann. Med. Intern. Fenniae.* 1947, v. 36, No. 1, 53–65, 4 figs. [11 refs.]

Diphyllobothrium latum is, the author says, very common in Finland, yet people infested with it seldom have anaemia. EHRSTROM, quoted by von Bonsdorff cited below, calculated that only 1 patient in 5,000 to 10,000 is ill with tapeworm anaemia, but SEPPÄ's (*Duodecim*, 1927, v. 43, 101) estimate is 1 in 659 and TÖTTERMAN's 1 in 113 to 1 in 383. SALTZMAN (*Acta Med. Scandinavica*, 1924, Suppl. 7, p. 268) and VON BONSDORFF [this *Bulletin*, 1940, v. 37, 215, 216 ; *ibid.*, 1944, v. 41, 593, 594 ; and *Nordisk Med.*, 1941, v. 12, 2877] ascribe this incidence either to " an abnormal character of the worm or to a ' constitutional ' disposition of the host." The latter explanation was supported by SCHAUMAN (quoted by von Bonsdorff and Saltzman), but has not been proved. The present author describes one case which, in his opinion, " indicates very clearly " that " the abnormal character of the worm " decisively influences the genesis of tapeworm anaemia. This case was a woman aged 23, whose anaemia disappeared after administration of filicin, which failed to remove the whole worm ; she had no anaemia when she returned 1½ years later for further treatment for removal of what the author considered to be the same tapeworm. He suggests that the anaemia in this case may have been caused by some " disease " of the tapeworm and that the anthelmintic may have cured this, so that the patient's anaemia disappeared.

Three other patients are also discussed, all of whom had free HCl, so that pernicious anaemia was absent. In all three cases, blood regeneration ceased after the worm cure and only continued when liver treatment was given. Examination of these cases 4, 6 and 7½ months respectively after cessation of the liver treatment showed that all were completely healthy. The author discusses these cases in relation to the view that *D. latum* destroys all the anti-anaemic liver factor at the patient's disposal and suggests the alternative hypothesis that the " worm poison has a paralysing effect upon the blood-forming organs, the bone-marrow and the liver ", which were strong enough in these 3 cases to begin regeneration of the blood, but not strong enough to complete this without the help of liver treatment. *G. Lapage*

BECMEUR, A. Situation de l'ankylostomiase du centre minier de Khouribga en 1945. [**The Ankylostome Problem in the Khouribga Mines in 1945.**] *Bull. Inst. Hyg. Maroc.* 1945, v. 5, 75–83.

In the phosphate mines at Khouribga in 1938, in two *recettes* [parts of a mine], 68·88 per cent. and 40·51 per cent. of the workers respectively had ancylostome infection ; it was heavy in 8·9 and 1·2 per cent., medium in 33·37 and 13·66, and light in 26·68 and 25·65 per cent. The number of healthy workers infected within 6 months was 65·93 and 20·17 per cent., respectively.

As a result of prophylactic procedures by the end of 1941, there were no heavily infected workers, only 21·7 and 16·1 per cent. of lightly infected carriers and the chances of contamination in 6 months were reduced to 9·9 and 3·6 per cent. respectively.

The remaining 109 lightly infected carriers in the two *recettes* had only an average of 10 eggs per ml. of stool and were healthy. During the next four years, their number was reduced to 70, 30, 13, and 6 successively, while the numbers of the workers had risen from 885 to 3,132. By 1945 no parasite-free workers became infected after working 6 months in the mines.

This improvement was achieved by two procedures: (i) the treatment of all the medium and heavy carriers, and (ii) the construction of double trench latrines, 1·50 metres wide by 3 metres deep, at various points in the mines so that no worker had to go more than 400 metres to use one.

The latrines and the surrounding earth were periodically disinfected with cresyl and chloride of lime, and the latrines were abandoned long before the contained faecal matter reached the level of the galleries.

For sterilizing the carriers, the author found *Essence de Niaouli* and oil of chenopodium quite useless, and male fern, thymol and carbon tetrachloride very inadequate. Tetrachlorethylene was reliable; he gave it in 1-gramme capsules for three days, 3 grammes on the first day, 4 grammes on the second and 5 grammes on the third, followed three hours after the last dose by 40 grammes of sulphate of soda. By this means he obtained expulsion of worms in 100 per cent., complete removal of infection in 87, and partial removal in 13 per cent. of those treated.

The author used the book on ancylostomiasis by GARIN, ROUSSET and GAUTHIER for constant reference, and adapted their teaching to the local conditions. *L. E. Napier*

PANTOJA, W. P. & BASSÈRES, M. S. Verminoses.—Tratamento em massa pelo hexyl-resorcinol. [**Mass Treatment of Worm Infections by Hexyl-Resorcinol.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, July, v. 1, No. 2, 251–60.

The English summary appended to the paper is as follows:—

"1. A total of 7,341 people, including all age groups from 2 years up were treated in mass treatment campaigns in labor camps and small villages in the states of Espirito Santo and Minas Gerais, during 1944 and 1945, using the hexyl-resorcinol 'crystoids'.

"2. In a group of 117 children, apparently healthy, living in a leprosarium preventorium, in which the mean egg-count (Stoll-Hausheer) showed 2,630 hookworm eggs per cc. two treatments by the standard dosages showed a reduction of 85·2 per cent. from the mean number of eggs found in the first examination. It is emphasized that in spite of the relatively low reduction of hookworm eggs, after two treatments, the hexyl-resorcinol should be the drug employed in rural areas where there is a high prevalence of associate hookworm and ascaris infections. The mass treatment campaign is the method of choice and should be built around the drug, to take full advantage of its atoxicity and remediate [*sic*—? compensate for] its apparently low reduction of hookworm following a single treatment.

"3. Except for extremely rare manifestations of slight abdominal discomfort, and some allergic reactions, probably due to dead ascaris, no untoward symptoms were observed."

i. DAVIDSON, A. G., BARON, Bessie & WALZER, M. **Factors influencing Reagin Formation in Experimental Human Sensitization to *Ascaris lumbricoides* Antigen. I. Influence of Chronic Infection (Tuberculosis) on Rate of Sensitization.** *J. Allergy.* 1947, Nov., v. 18, No. 6, 359–68, 3 figs.

ii. KAILIN, Eloise W., DAVIDSON, A. G. & WALZER, M. **II. The Influence of Sex as a Factor in Rate of Sensitization.** *Ibid.* 369–72, 1 fig.

iii. ——, —— & ——. **III. The Influence of Race as a Factor in Rate of Sensitization with further Observations on the Sex Factor.** *Ibid.* 373–80, 3 figs.

This is a study on allergy, and the relation to *Ascaris* infection is not considered.

i. FÜLLEBORN and KIKUTH [this *Bulletin*, 1930, v. 27, 956] and others have shown that sensitization of the skin to *Ascaris lumbricoides* could be induced in man. The antibodies responsible for the immediate skin reactions in *Ascaris* hypersensitiveness are atopic reagins.

In these studies the extract was prepared from *Ascaris lumbricoides* (pig). The worms were first washed in water, afterwards in toluol. "They were then covered with a slight excess of buffered saline and with a layer of toluol. This was allowed to stand at room temperature until most of the worms had disintegrated. The material was paper-filtered and sterilized by Seitz filtration on June 2, 1933. The extract was bottled, covered with a layer of toluol, and stored in the ice box. On September 3, 1935, it was again passed through a Seitz filter. At this time the total nitrogen content determined by the macro-Kjeldahl method was 5·3 mg. N per ml. From this stock material, proper dilutions for use in this study were made."

The experimental subjects were selected by giving a test dose of 0·025 ml. of an extract containing 0·1 mgm. of N per ml. Only persons giving a negative reaction were used. Sensitizing doses of 0·1 ml. were given at intervals of one week until complete sensitization was effected, or 12 doses had been given. A positive reaction was indicated by the formation of a weal and erythema.

About one-third of the persons given the test dose showed positive or doubtful reactions and were excluded from the experiment.

The sensitization developed in the rest at a variable rate: 19 per cent. became sensitive at the time of the third sensitizing dose (S_3), 54 per cent. at S_5, 81 per cent at S_2, and 92 per cent. at S_{12}.

Chronic tuberculous infection was not a factor influencing the rate of development of sensitivity, but sensitivity developed more rapidly in males than in females. The number of positive reactions was higher by about 25 per cent. in males than in females between the S_4 and S_8, but the final percentages, *i.e.*, at S_{12}, were equal in the two sexes.

ii. The observation made in the earlier investigation that active sensitization to *Ascaris* antigen develops earlier in the male was confirmed, and it was incidentally indicated that there is earlier sensitization to the antigen in the Negro race than in white persons.

iii. Further confirmation was obtained of the earlier sensitization to *Ascaris* antigen of negroes compared with white persons and males compared with females. There was no correlation between the rate of sensitization and the natural sensitivity in the four population groups, which was undoubtedly, but not demonstrably, associated with present or past helminthic infection. There was no correlation between rate of sensitization and age. *L. E. Napier*

FRANKS, M. B., CHENOWETH, B. M., Jr. & STOLL, N. R. **Reactions of Natives of Okinawa and of American Personnel, to Skin Tests with Test Antigen prepared from Microfilariae of** *Dirofilaria immitis*. *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 617–32, 3 figs. & 2 graphs. [18 refs.]

After a brief review of the relevant literature, the authors describe skin tests done from July to October, 1945, on the island of Okinawa. Antigens were made from the adults (females only) and microfilarial larvae of *Dirofilaria immitis* of the dog and from *Ascaris lumbricoides* obtained at necropsies in a Guam hospital. For the methods of making these antigens, the paper must be consulted. *Trichinella spiralis* antigen was supplied by the National Institute of Health. This and saline containing 1/10,000 merthiolate (used to preserve the other antigens) were used as controls. References are given to the methods of counting the helminth eggs in faeces, and the number of microfilariae.

Skin tests were done on more than 400 patients in two natural groups. Group I were service personnel. Sixty of them, stationed on Guam, had not previously been outside the U.S.A. and were not known to have been in areas in which filariasis is endemic ; fifty-three had no intestinal helminths, 7 were lightly infected with these. Group I included also 9 patients with a clinical diagnosis of filariasis. Group II consisted of natives of the endemic area of Okinawa considered to be fairly representative of the island's population.

Details are given of the method of doing the skin tests and other examinations of the patients. Examination of a random sample of 677 Okinawans showed that 26·6 per cent. had circulating microfilariae and that 57 per cent. of 259 Okinawans with this degree of microfilaraemia had physical signs attributable to filariasis. A table illustrates the increased incidence of physical signs with increasing ages, a fact which was considered in the interpretation of the skin tests. Diagnosis was conservatively made on involvement of lymph nodes and channels, the extremities and the scrotum and may have placed the incidence of physical signs too low. Only 8 persons examined (rather more than 1 per cent.) had elephantiasis, which was no functional handicap to 4 of the 8. As only 20 other cases of elephantiasis were seen and only one of these was multiple, the usual assumption that filarial infestation and elephantiasis go hand in hand was not confirmed in Okinawa. Combined blood and chemical studies indicated a demonstrable incidence of filariasis in Okinawa of 65 per cent. and probably this is considerably higher. The authors concluded, in fact, that they were justified in considering all Okinawans, except very young infants, to be infected.

No intact adult worms were found, but the nocturnal periodicity of the microfilariae and examination of stained smears of them showed that the infecting species was *W. bancrofti*. Microfilarial counts of blood drawn between 8 and 10 p.m. from 180 patients varied from 1 to 23,000 microfilariae per ml. ; 80 per cent. of cases had 1,000 or less per ml. and only 6 per cent. had 4,000 or more per ml. Positive examinations for microfilariae increased significantly with age, especially when children of 6 to 15 years (19 per cent.) were contrasted with adults aged 46–74 years (34 per cent.), the corresponding figures for incidence of physical signs in patients with microfilaraemia being 38 per cent. and 95 per cent. and in patients without microfilaraemia 40 per cent. and 73 per cent. There was no positive correlation between the numbers of circulating microfilariae and either the age of the patients or the degree of clinical filariasis. Of the 8 patients with elephantiasis, 4 had circulating microfilariae, but in 3 of these the elephantiasis was minimal (*cf.* above).

For details of the results of the skin tests the paper itself must be consulted. An important net result was the confirmation of the conclusion of earlier workers that an antigen made from microfilariae of *D. immitis* " has a limited use as a diagnostic aid in filariasis. It is more specific in the sense that fewer false

positives are elicited by it in non-filarial persons than are provoked by antigens made from adult female *D. immitis*. For this reason it may be used at stronger concentrations and in this report was employed at 1 : 1000 as compared to 1 : 1,800 for adult worm antigen." Thus, "on a basis of dry weight of lyophilized antigen, the microfilarial antigen gives 90 per cent. fewer false positive reactions in normal controls and in patients with intestinal helminthiasis than does the antigen made from female adult *D. immitis*."

The reactivity of the test antigen is apparently influenced by the clinical stage of the disease. In 320 natives of Okinawa only 61 per cent. gave positive responses to the microfilarial antigen and it was remarkable that most of the negative skin reactions were given by the group *with* circulating microfilariae. Thus only 20 per cent. of the Okinawans without circulating microfilariae gave negative reactions. A negative reaction occurred as often when the microfilariae counts were low as when they were high and, when positive skin tests occurred in the group with microfilariae, they were slight.

The older age groups gave more negative reactions, so that an age resistance was demonstrated which is, the authors think, a measure of the immunity developed in relation to the length of time of exposure to the infection and to its degree. A striking illustration of this is the fact that practically all the patients with elephantiasis gave negative reactions. The results suggest that persons infected for 4–6 months have not yet produced much antibody to the larvae and that presumably at this early stage only antibody to the adult worm is being produced.

The occurrence of positive reactions to *Trichinella* antigen in a population in which there is no evidence of *Trichinella* infection is discussed.

A circulating antigen has been demonstrated which partly explains the responses obtained and is discussed elsewhere by FRANKS [this *Bulletin*, 1947, v. 44, 446]. *G. Lapage*

HEWITT, R. I., WALLACE, W. S., WHITE, E. & SUBBAROW, Y. **Experimental Chemotherapy of Filariasis. I. Experimental Methods for testing Drugs against naturally acquired Filarial Infections in Cotton Rats and Dogs.** *J. Lab. & Clin. Med.* 1947, Nov., v. 32, No. 11, 1293–303. [23 refs.]

In the testing of filaricides in the laboratory, the usual laboratory animals employed are the dog and the cotton rat. The authors report on the methods employed by them in routine testing of a large series of non-metallic organic compounds against filarial infections occurring naturally in these hosts, *i.e.*, *Dirofilaria immitis* and *Litomosoides carinii* in the dog and cotton rat respectively.

A method is described of estimating the fluctuations in the numbers of microfilariae in the peripheral blood of cotton rats over a number of weeks. In a series of rats examined by this method, a marked increase in the numbers of microfilariae was observed and in only one untreated rat out of sixty-five the microfilarial count dropped spontaneously to zero. The significance of this observation in relation to treated animals is commented upon. Of 65 rats examined post-mortem, nine showed a small number of dead worms and in no case were large numbers of dead worms found.

Compounds for testing were administered orally or intraperitoneally to cotton rats, depending on their solubility, in experimental dosages which determined the frequency of subsequent treatment. Autopsies were performed from two to four weeks after cessation of treatment, depending on the activity of the compounds, suggested by previous tests. In view of the lack of knowledge of the

mode of action of filaricides the trial and error method of approach seemed the most commendable one.

In experiments with dogs, heavily infected animals were considered poor risks for treatment, since large numbers of worms, if killed quickly and simultaneously may produce an embolus in the pulmonary artery and kill the dog. On the other hand, dogs (as well as cotton rats) with low initial microfilarial counts are unsatisfactory for assay purposes. These animals were used only in testing compounds which had shown activity in the cotton rat, in dosages derived from experience of their tolerance in cotton rats.

Three criteria were used in determining the effectiveness of new compounds against *Dirofilaria* in dogs, (1) a rapid and sustained reduction in microfilariae, (2) presence of dead worms in the terminal blood vessels within the lungs at autopsy, and (3) improved physical condition of the dogs.

Of 517 organic non-metallic compounds which were tested, several types showed activity in the cotton rat, but the best balance between activity and toxicity was found in the piperazines, administered orally or intraperitoneally. Detailed results of the effects produced by piperazine derivatives are presented in subsequent papers [see below]. *J. J. C. Buckley*

Hewitt, R. I., White, E., Wallace, W. S., Stewart, H. W., Kushner, S. & SubbaRow, Y. **Experimental Chemotherapy of Filariasis. II. Effect of Piperazine Derivatives against naturally acquired Filarial Infections in Cotton Rats and Dogs.** *J. Lab. & Clin. Med.* 1947, Nov., v. 32, No. 11, 1304–13.

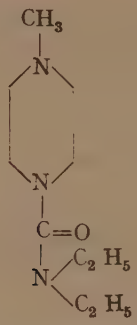
The authors found that several members of the piperazine group produced precipitous reductions in the microfilarial counts in cotton rats after various oral or intraperitoneal doses. Of these derivatives, 1-carbethoxy-4-methylpiperazine hydrochloride (compound 180-C) was consistently effective and was at first used as standard in the treatment of 81 cotton rats. Detailed results of this series are tabulated. Compound 180-C was markedly effective against microfilariae in cotton rats in well tolerated doses but its effect against adult worms was not as promising. In dogs, the dosages which reduced microfilariae had adverse effects on the dogs themselves. However, another compound 1-diethylcarbamyl-4-methylpiperazine hydrochloride (84-L) was subsequently chosen as standard, and was effective in reducing microfilariae in doses as low as 3 mgm. per kilogram in cotton rats, and produced no toxic effects in dogs, in therapeutic doses. Furthermore, frequent administration of compound 84-L resulted in the death of a large proportion of adult worms in cotton rats.

A detailed report on this compound is given in another paper in this series [see below]. *J. J. C. Buckley*

Hewitt, R. I., Kushner, S., Stewart, H. W., White, E., Wallace, W. S. & SubbaRow, Y. **Experimental Chemotherapy of Filariasis. III. Effect of 1-Diethylcarbamyl-4-Methylpiperazine Hydrochloride against naturally acquired Filarial Infections in Cotton Rats and Dogs.** *J. Lab. & Clin. Med.* 1947, Nov., v. 32, No. 11, 1314–29.

Detailed data are presented showing the effects produced by 1-diethylcarbamyl-4-methylpiperazine hydrochloride (compound 84-L) on

natural infections with filarial worms of cotton rats and dogs. The structural formula of compound 84-L is given below :—



Two hundred and twelve cotton rats and twenty-five dogs were used in testing this compound against both the microfilariae and the adult filariae. After oral or intraperitoneal treatment of filaria-infected cotton rats, at doses ranging from 3 to 100 mgm. per kilogram, the microfilarial count dropped suddenly within 24 hours and became negative or remained very low as long as treatment continued. *In vitro* experiments led to the conclusion that the compound acts directly on the microfilariae in the blood. The rate of disappearance of microfilariae in dogs is not so rapid as in cotton rats, but in one to two weeks over 90 per cent. generally disappear.

The effect of the compound on adult filariae in cotton rats varied with (1) the amount of drug given, (2) the frequency of the dosage and (3) the number of days elapsing from cessation of treatment to autopsy. Of 150 rats treated with 10 mgm. per kilogram at least twice daily, 72 per cent. showed either some or all adults dead at autopsy ; but dosage three times daily was shown to give more consistent results.

In general, animals treated with less than 10 mgm. per kilogram did not exhibit as many dead worms at autopsy as those treated with 10 mgm. or more per kilogram. Usually the longer the period between cessation of treatment and autopsy, the fewer live worms were found on autopsy. Oral and intraperitoneal treatment of dogs with compound 84-L was encouraging in that doses necessary to affect the microfilarial counts and in some cases, to affect the adult worms, did not produce signs of severe toxicity. Detailed data of the results of treatment of 25 filaria-infected dogs are tabulated. Although the optimum treatment schedule has not yet been determined, it appears that frequent administration of the drug for several weeks is desirable.

J. J. C. Buckley

VAN HOOF, L., HENRARD, C., PEEL, E. & WANSON, M. Sur la chimiothérapie de l'Onchocercose. (Note préliminaire.) [**The Chemotherapy of Onchocerciasis : Preliminary Note.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Mar. 31, v. 27, No. 1, 173–7.

Since 1944 the authors have systematically tested various drugs for curative action in onchocerciasis :—oil of chenopodium, eucalyptine, thymol, commercial pyrethrins, antimonials, atebrin and Tryparosan. Only the last gave indication of usefulness, and its effect was transient. This, however, encouraged the authors to try the organic trypanocidal drugs, especially Antrypol (or Belganyl). In 1942, moreover, two volunteers for (successful) experimental infection with *O. volvulus* also volunteered for infection with trypanosomes, and were treated

with Antrypol ; more than two years afterwards they were found free, not only from trypanosomiasis, but also from onchocerciasis.

The authors have treated with Belganyl a series of patients suffering from onchocerciasis. At first they gave two doses, each of 2 grammes, each week, but after the second or third injection there was often an intense reaction, with fever, severe articular pains, pruritus about the skin lesions, and massive exfoliation, and pain in the onchocercal tumours. Patients with eye involvement showed conjunctival reactions. Later the authors found that a total dose of 7 grammes, given at the rate of 1 gramme each week, was usually enough to cause disappearance of microfilariae and macrofilariae within 1–2 months ; a total dose of 10 grammes appeared always to be successful. Dead adult filariae, containing dead and degenerated embryos, are found in the tumours. The authors found appreciable amounts of the drug in cysts, even 6 months after the last injection.

Fuller details of this work are to be published later. *Charles Wilcocks*

STRYKER, W. A. **The Intestinal Phase of Human Trichinosis.** *Amer. J. Path.* 1947, Sept., v. 23, No. 5, 819–27, 4 figs. on 2 pls. [27 refs.]

There are few records of the discovery of adult *Trichinella spiralis* in the intestine of man. The author gives 7 of these. A few of them are confirmed by microscopical examination. Persistence of adult *Trichinella* in this situation has been recorded for 30 days, but not longer. Work on trichiniasis of experimental animals, especially that done by ROTH (*J. Parasitology*, 1938, v. 24, 225) suggests, however, that the female *Trichinella* produces larvae for about 6 weeks.

The author reports on a man, aged 35, who had acquired trichiniasis from raw pork sausage prepared from a hog raised and butchered by himself. Other members of his family were also infected and his daughter, aged 8, died. The patient's wife and the family doctor said that raw pork had been eaten once only, the father and daughter having eaten more than the others did.

The father had diarrhoea, marked muscular pain, fever and terminal respiratory distress. There were physical and electrocardiographic signs of myocardial damage and neurological abnormalities which suggested cerebral damage. Death occurred 54 days after eating the pork. Adult male and female *Trichinella* were found microscopically in many sections of both the large and small intestine, being more numerous in unopened portions of the intestine, whose contents were not disturbed. Most of the females contained larvae. The nematodes were free in the lumen or embedded in the mucosa, one having penetrated as far as the *muscularis mucosae*, though none penetrated further than this. Often one end was in the mucosa, the remainder projecting into the lumen. Most often the " uterine area " of the *Trichinella* was embedded in or in contact with the mucosa, which showed no significant cellular reaction around the worms, lymphocytes or plasma cells and eosinophils being found elsewhere in the mucosa at a distance from the worms and also in control cases not infected with *Trichinella*. In the intestine granulomatous infiltration, haemorrhage or foci of necrosis were not found, but the infestation of skeletal muscles was unusually heavy, larvae being present even in the cremaster muscle of the spermatic cord. Single muscle fibres contained as many as 3 larvae at the level of a single section. Some larvae were still straight, but most were coiled and cyst formation had begun. Many muscle fibres showed hyaline degeneration and between them there was a heavy cellular infiltration of mononuclear macrophages, lymphocytes, plasma cells and many eosinophils. A few foci were purulent. Dr. S. E. Gould found 2,677 larvae per gramme of diaphragmatic muscle, which is one of the heaviest infestations known. The

heart and brain showed typical trichinous myocarditis and encephalitis, larvae being found in both these situations. Photomicrographs illustrate this.

The author briefly discusses the resistance of various hosts to *T. spiralis*, suggesting that man is relatively susceptible and that the intestinal phase of the first infection may be prolonged, because there is no acquired resistance, and that infection with relatively large numbers of larvae may also prolong the intestinal phase. These were features of the case reported and they are correlated with the fact that the period of persistence of the adults in the intestine was one of the longest ever reported and larvae were still being released 54 days after infection. Persistence of the intestinal phase means persistence of the myositis and increased severity and duration of the myocarditis and encephalitis, death during the acute phase being usually due to lesions of the heart and central nervous system. These organs are affected only by migrating larvae, which do not encyst in them, so that inflammation of these organs subsides when the larvae move on. Thus, in the case reported, larvae were found in the heart and brain, in both of which there was granulomatous infiltration.

Attempts to remove the worms from the intestine are therefore important. The author thinks anthelmintics are of little use and recommends (with references to the literature) purgation, attention to the patient's fluid balance and general condition and administration of immune and convalescent sera which may affect the larvae and reduce the number of adults. *G. Lapage*

DEFICIENCY DISEASES

HANAFY, M. **The Subacute Subnutritional Syndrome in Infants.** *J. Roy. Egyptian Med. Ass.* 1947, Sept., v. 30, No. 9, 440–50, 18 figs. on pls.

Malnutrition in infants may present numerous different clinical pictures. The author believes that these are all stages in the development of a single syndrome. This conclusion is based on the study of 197 cases, mostly between the ages of one and three years, all of whom had been fed for some months on a diet consisting only of rice or cereal water.

Four grades of severity are distinguished :

1. Weight loss up to 15 per cent. with or without signs of riboflavin deficiency.
2. Weight loss from 15 to 30 per cent., with irritability, diminished reflexes, and a dry, inelastic skin. Oedema may be present.
3. Weight loss from 30 to 50 per cent. In some cases there are pellagrous skin lesions, in others an enlarged tender liver (pre-ascitic stage of cirrhosis).
4. Weight loss more than 50 per cent. Cirrhosis of the liver may be present with or without pellagrous lesions.

Only the more severe grades are described in detail. The picture corresponds closely to that of kwashiorkor in West Africa or infantile pellagra in South Africa. Some additional features were found. Bronchiectasis was present in 5 per cent. of cases. Carpopedal spasm, suggestive of tetany, was sometimes observed, although the blood calcium did not fall below 8 mgm. per cent. In some cases the bones showed " a definite clinical picture of rickets ". The stools sometimes contained blood, pus and mucus. Three cases resembled Von Jaksch's syndrome, with splenomegaly, leucocytosis, and anaemia.

Early cases responded to treatment with a high protein diet and vitamins. In the more severe grades, nicotinic acid and vitamin B_1 were ineffective.

In agreement with the observations of GILLMAN [this *Bulletin*, 1946, v. 43, 237] administration of one factor alone made the general condition worse. Good results were obtained with vitamin B complex (the form is not stated) and with crude liver extract, and best of all with these two together. Parathyroid hormone, first tried because of tetany, was also found to enhance the action of liver extract.

No figures of mortality rate are given, and little is said of prognosis except for the important point that the prognosis is not affected by the presence or extent of either oedema or pellagrous skin lesions.

Analysis of the symptoms and of the response to treatment suggests that the disease is the result of a multiple deficiency—of protein, vitamin B complex, and vitamins A, C, and D. To these may perhaps be added deficiency of unidentified factors present in liver extract. In late cases there may be a change in endocrine function, which can only be restored by replacement therapy with hormones.

[This paper is illustrated by many striking photographs. It is the first description of the kwashiorkor syndrome that has appeared from Egypt: as such it is important in view of the earlier suggestion that the disease occurs only in children of negro stock. In Egyptians, the syndrome appears to be unusually well-developed, covering almost the whole range of known deficiency states, since in some cases there was evidence of rickets and of vitamin A deficiency. These conditions are not part of kwashiorkor as it occurs in the tropics, although they were present in some cases described by Gil in Mexico.

In kwashiorkor the liver is typically fatty. Dr. Hanafy's mention of cirrhosis with ascites raises interesting speculations. It is to be hoped that the results of post-mortem examinations will be published.]

J. C. Waterlow

GLUSMAN, M. **The Syndrome of "Burning Feet" (Nutritional Melalgia) as a Manifestation of Nutritional Deficiency.** *Amer. J. Med.* 1947, Aug., v. 3, No. 2, 211–23. [50 refs.]

HO, T. T. Een klinische observatie omtrent beri-beri onder het werkvolk in Tandjong-Priok in de Japanse bezettingstijd. [**Clinical Beriberi in Batavia Port during the Japanese Occupation.**] *Med. Maandblad.* 1947, Dec., No. 17, 326–31. English summary.

This investigation relates to the examination of 1,000 recruits for work in the harbour of Batavia and not to applicants for admission to hospital. Already this labour population, after 9 to 12 months of Japanese occupation, showed bodily deterioration. Out of the thousand coolies examined, 157 were found suffering from severe beriberi with serious cardiovascular symptoms, and large numbers suffered from slighter degrees. It was especially noteworthy, and by previous standards the reverse of expectation, that 150 out of the 157 showed dry beriberi and only 7 wet beriberi. This leads the author to ask whether dry beriberi is not explainable as a partial thiamin deficiency and whether there is present in thiamin an anti-oedema factor. The clinical signs of dry beriberi are given in detail and it was noted that the calf muscles were neither swollen nor painful; reflexes were heightened; there might even be clonus, and the patellar and *tendo achillis* reflexes were especially marked. Rapid response to treatment with thiamin is illustrated by reference to 14 specially selected cases.

A general summary of the deductions made is presented as follows: In place of the classical beriberi triad of (1) oedema, (2) heart and vessel symptoms, (3) polyneural degeneration, the author gives the following description:—

" Aneurin-deficiency leads to degenerative changes of peripheral nerve twigs, chiefly restricted to two regions, those of (*a*) the peroneal nerve and the tibial nerve, (*b*) the vagus nerve and vasomotor twigs. The predominance of the lesions in one or other or both of these two regions represents the clinical distinction between wet and dry beriberi ". *W. F. Harvey*

SPRUE

FOURMAN, L. P. R. **The Chylomicron Count in Normal Subjects and Patients with Sprue.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 537–44. [10 refs.]

After a fatty meal, the serum has a characteristic milky appearance, and under dark-ground illumination numerous fine particles, less than 1μ in diameter, are seen in a state of Brownian movement. These chylomicrons consist of neutral fat with an outer layer of globulin. Particle counts are made on a small drop of serum spread out by pressure between slide and coverslip. They are estimated in terms of the number of particles per standard field.

In an investigation on fat absorption in sprue, counts were made before and after a meal of 200 ml. of homogenized evaporated milk containing 18 gm. of fat. Chylomicron counts in individual cases were compared with the percentage fat absorption on a controlled diet, and with blood fat and glucose-tolerance curves. Eighty-seven curves were constructed on data from 28 patients with sprue, and these were compared with eighteen curves on eleven normal subjects. With a meal containing 18 gm. of fat, the peak counts in normal persons ranged between 100 and 270 particles per standard field. The chylomicron curve in normal persons increased and diminished when more or less fat was given, suggesting that they do at least represent one form of absorbed fat. On the other hand, low curves were produced in normal persons by giving calcium lactate with the meal; in fat balance experiments calcium lactate did not produce steatorrhoea. When " flat " chylomicron curves returned to normal with clinical improvement, there was no corresponding diminution in the steatorrhoea. Chylomicrons were shown to represent a variable fraction of the absorbed neutral fat in the serum. In untreated sprue, low curves were found in about half of the patients examined. After 2 or 3 weeks of parenteral liver therapy, patients whose curves had been low gave normal curves.

It is concluded that a small proportion of the total fat is absorbed without splitting, as finely emulsified fat.

Whilst all patients with sprue have a defective absorption of split fat, only some show impaired neutral fat absorption as judged by the chylomicron count. Failure to absorb neutral fat is more common in the severe cases and responds to liver therapy. *P. Manson-Bahr*

SPIES, T. D., GARCIA LOPEZ, G., STONE, R. E., MILANES, F., BRANDENBURG, R. O. & ARAMBURU, T. **Further Observations on the Specificity of the Folic Acid Molecule.** *Blood.* 1948, Jan., v. 3, No. 1, 121–6, 9 figs.

" Methyl folic acid, N-(4-(4-quinazoline)amino)benzoyl)-glutamic acid, the Mg salt of formyl pteroyl glutamic acid, the Mg salt of formyl pteroic acid, pteroyl aspartic acid, oxyfolic acid and oxypteroic acid have been studied as to their effect on blood regeneration in selected cases of Addisonian pernicious anemia, nutritional macrocytic anemia and tropical sprue. In the amounts administered, only the Mg salt of formyl pteroyl glutamic acid was effective

in producing reticulocytosis and an increase in red blood cells, hemoglobin, white blood cells and platelets, and it was not as effective per unit of weight as was folic acid per se. Presumably this compound is slowly changed into folic acid in the body. It is of special interest that the Mg salt of formyl pteroic acid (Streptococcus lactis factor) was negative in producing hemopoiesis. These observations show the very great specificity of the folic acid molecule."

Darby, W. J., Jones, E., Warden, H. F. & Kaser, Margaret M. **The Influence of Pteroylglutamic Acid (a Member of the Vitamin M Group) on Gastrointestinal Defects in Sprue. A Study of Interrelationships of Dietary Essentials.** *J. Nutrition.* 1947, Dec. 10, v. 34, No. 6, 645–60, 5 figs. (1 coloured). [43 refs.]

Patients with the complete sprue syndrome may exhibit remarkable combinations of deficiency states. Some of these manifestations are: loss of weight (calorie deficiency); hypoproteinaemia (protein deficiency); petechiae (vitamin K or C deficiency); night blindness and xerosis conjunctivae (vitamin A deficiency); hypocalcaemic tetany and osteoporosis (vitamin D and calcium deficiency); and pancytopenia (vitamin M deficiency). In many cases these deficiencies may be classified as latent or potential.

With the demonstration of the activity of pteroylglutamic acid (PGA) [folic acid] in sprue patients, it has been indicated that this vitamin exerts a favourable influence upon the gastro-intestinal abnormalities, as well as upon the anaemia. In this paper additional evidence is adduced that PGA does so.

Six adult patients were under observation and all demonstrated the diagnostic criteria. The sole specific drug administered was synthetic PGA in doses of 5 mgm. daily by the mouth or 15 mgm. intramuscularly, except in one patient in whom this was preceded by 10 days' therapy with pteroyltriglutamate. During treatment one was on a meat-free diet, but the remainder were on a regular ward diet.

During each relapse, the patients complained of glossitis, and all showed atrophy of lingual papillae. Subjective relief of glossitis resulted and the commencement of regeneration of papillae was evident within 3 days to one week. In relapse, the same succession of events took place. If the appearance of the tongue is an indication of the state of the gastro-intestinal tract, then it can be inferred that this vitamin exerts the same beneficial action on the mucosa.

In all remissions cessation of diarrhoea was observed within a period of 3–9 days from the beginning of PGA therapy.

The maximum gain in weight varied from 6 to 45 pounds. The impression gained is that these weight changes were the result of increased appetite and better absorptive capacity of the gastro-intestinal tract.

As regards glucose tolerance (oral administration) there was a definite return towards the normal type of curve within 11 to 30 days after the institution of therapy. It is permissible to suggest that PGA assists the permeability of the gastro-intestinal tract to glucose.

The control of fat intake of patients is difficult. Observations on the effect of PGA on faecal fat were limited, but successive determinations on a single patient indicated a definite decrease in the 24-hour loss of fat in the stool; but in chronic sprue the reduction of fat in the stool did not exceed that obtained with liver extract therapy.

A rise in serum carotene after PGA has already been demonstrated [this *Bulletin*, 1947, v. 44, 608] and may be attributed to accumulation, owing to ability to absorb the pigment. A sustained rise was registered in 6 of the 7 remissions.

Vitamin A absorption determinations after an oral dose of 200,000 I.U. have shown that improved absorption had taken place in 2 out of 4 remissions studied. The hypoprothrombinaemia in sprue is attributed to deficiency of vitamin K. Two patients with hypoprothrombinaemia, before PGA therapy, became normal during remissions.

The decrease in serum tocopherol (vitamin E) concentration during a sprue relapse, as well as an increase after PGA administration are shown by graphs. There is a contrast between concentrations of fat-soluble vitamin E in patients with sprue and in those with pernicious anaemia.

X-ray changes of the so-called deficiency pattern type are present in sprue. In 3 out of 4 follow-up films in remissions induced by PGA, a definite improvement in the pattern occurred.

The observations may be interpreted as indicating that the primary defect in sprue is a deficiency state which is corrected by PGA. The numerous interrelationships of PGA with other vitamins and food factors are a remarkable clinical example of similar relationships of foodstuffs in man and closely resemble the multiple deficiency states in the sulphonamide-treated rat.

As many cases of chronic sprue undoubtedly develop irreversible changes in the gastro-intestinal tract, and as degenerative changes in the intrinsic nerve plexuses have been demonstrated, it is improbable that they can be restored. Therefore the persistence of some degree of malfunction may be expected despite therapy.

Any disease which produces malabsorption from the gastro-intestinal tract may resemble the sprue syndrome and it is to be expected that PGA will be ineffective in the treatment of any disease which does not result from a deficiency of this vitamin : this factor should enable clinicians to separate the different clinical conditions which are loosely grouped together as the sprue syndrome. Regarding the possible synthesis of vitamins by the bacterial flora of the gastro-intestinal tract, it has been observed that during PGA therapy a normal flora has been re-established in sprue. It is obvious that much more careful studies will be needed to define the relative rôles of altered gastro-intestinal absorption, metabolism and gastro-intestinal synthesis in the pathogenesis of the manifold deficiencies observed in sprue.

P. Manson-Bahr.

HAEMATOLOGY

Spies, T. D., Garcia Lopez, G., Stone, R. E., Milanes, F., Toca, R. L. & Aramburu, T. **Treatment of Nutritional Macrocytic Anaemia with Synthetic Folic Acid.** *Lancet.* 1948, Feb. 14, 239–41, 2 figs.

Two important advances have been made recently in the discovery that folic acid produces a prompt haemopoietic response in nutritional anaemia and that 5-methyl-uracil (thymine), when given in several thousand times the dose, produces a similar response. For the purposes of this study, 32 persons with nutritional macrocytic anaemia, all Europeans, aged 35–70, the majority being males, were selected. In this arbitrary selection, the following criteria were employed : the red cells were fewer than 3,000,000 per cmm. : the bone marrows showed the typical erythroblastic arrest : repeated gastric analyses showed free hydrochloric acid in the gastric contents, while the icteric index was normal and no recent treatment had been given.

Rigid dietetic control in hospital consisted of the exclusion of meat, meat products, poultry and fish, while detailed histories showed that the diets of these patients had been grossly deficient in protein and the vitamin B complex for many years. All patients had lost weight and complained of tiredness and in all diarrhoea had been present from one to three months.

Pain, burning and sensitivity of mouth and tongue were common and many had paraesthesiae and hypoaesthesia. Oedema, associated with a reduction of serum-albumin was present in 9, pellagra, scurvy, riboflavin deficiency and aneurin and ascorbic acid deficiencies in others.

After folic acid treatment, reticulocytosis, increase in haemoglobin and in erythrocytes indicated a satisfactory response in every case. Follow-up studies for eighteen months have shown that none had a severe relapse. The response was adequate to 10 mgm. of folic acid daily, which was continued in some patients for as long as 77 days. In contrast to patients with Addisonian pernicious anaemia, no evidence of development of subacute combined degeneration of the cord was obtained. The blood-levels were maintained for eighteen to twenty-four months with no other specific therapy.

P. Manson-Bahr

COWAN, G. A. B. **Folic Acid in Severe Nutritional Anaemia: a Report of Five Cases.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Jan., v. 41, No. 4, 525–35, 5 figs.

Severe anaemia in Malaya is responsible for much ill-health and many deaths. The causes are malaria, helminthic infection, malnutrition and chronic infections. Out of 142 cases, 24 were found to have red-cell counts of less than one million per cmm. Analysis of these showed that nutritional macrocytic anaemia accounted for nine (three associated with pregnancy), dimorphic anaemia for fourteen and iron-deficient anaemia for one only.

A nutritional factor, apart from iron, was thus concerned in 23 cases, and five of these were treated with oral synthetic folic acid. The total folic acid given was from 160 to 560 mgm. in from 16 to 42 doses. Reticulocytes reached their peak on about the 7th day of treatment. In each case the response to treatment was satisfactory: in two it was dramatic; both of these were examples of dimorphic anaemia.

P. Manson-Bahr

VENOMS AND ANTIVENENES

SERGENT, Et. Sérothérapie antiscorpionique (dixième note). Observations médicales reçues pendant l'année 1946. [**Anti-Scorpionic Serotherapy. X. Medical Reports received in 1946.**] *Arch. Inst. Pasteur d'Algérie.* 1947, June, v. 25, No. 2, 94–7.

During the year, 868 patients were treated, according to instructions, for scorpion sting; all survived except 4 of the group (124 in number) whose symptoms were alarming and in whom life was endangered. In addition there were 3 deaths in infants who were not treated, and 12 in persons treated with insufficient serum, or too late. The total figures since 1936 are 3,089 treated, of whom 655 showed grave symptoms; of these 655 patients, 592 (90·3 per cent.) were cured.

The author points out that patients should be kept under observation for several hours after administration of the serum, even if the symptoms have disappeared, because occasionally the improvement is apparent only, and there

may be a return of symptoms, and death. Instructions are given that if symptoms are severe, at least 20 cc. of serum should be injected, and repeated if there is no improvement in one hour, and again, several times, if necessary. A return of symptoms indicates another injection.

The scorpions were identified in 39 cases :—

23 *Prionurus australis*
11 *P. amoureuxi*
1 *P. quinquestriatus*
4 *Buthus occitanus*

[See also this *Bulletin*, 1947, v. 44, 534, 535.] *Charles Wilcocks*

SERGENT, Et. Intervalle de temps qui peut s'écouler entre l'injection de sérum antiscorpionique et la sédation des symptomes d'envenimement. [**The Time between Injection of Anti-Scorpionic Serum and Alleviation of Symptoms.**] *Arch. Inst. Pasteur d'Algérie.* 1947, June, v. 25, No. 2, 98–100, 1 graph.

A study of the symptoms of scorpion sting, in 209 cases in which the patients' condition was serious before injection of serum, shows that alleviation of the local pain, vomiting and sweating occurred within one hour of the injection of serum in 45 per cent. In almost all cases the improvement was evident within 6 hours, though in a very few it was delayed, even as long as 19 hours after the injection. *Charles Wilcocks*

DERMATOLOGY AND FUNGUS DISEASES

VANBREUSEGHEM, R. Importance des affections dermatologiques chez les Européens au Congo Belge. [**The Importance of Skin Diseases in Europeans in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1947, June 30, v. 27, No. 2, 251–5.

The author reviews the cases of skin affections found among a small European population of about 206 persons, residing in a fairly humid region of the lower Congo from December, 1942 to December, 1943.

By means of a graph showing monthly rainfall and the percentage of skin cases among his total consultations, he demonstrated that skin diseases account for about 20 per cent. of the morbidity rate and are most prevalent in the rainy months.

Mycotic and pyogenic affections comprise about 25 per cent. of the total.

C. C. Chesterman

HADLER, W. A. Classificação do pênfigo foliáceo baseada em dados anatomo-clinicos e hematológicos. [**Classification of Cases of** *Pemphigus foliaceus.*] *Arquivos de Dermat. e Sifiligrafia de São Paulo.* 1947, Mar.–June, v. 11, Nos. 1/2, 29–56, 21 figs. & 1 graph. [21 refs.] English summary.

Several classifications of this disease have been proposed : that of VIEIRA according to the course—hyperacute, acute, subacute and chronic, but the last is subdivided on a pathological basis into bullous, pustular, papillomatous, pigmented, herpetiform, etc. ; that of RABELO into 3 clinical types—erythemo-exudative, herpetiform, and exfoliative bullous ; that of ORSINI into benign

(*formes frustes*), with scattered lesions, or circumscribed (the Senear-Usher syndrome), and the severe generalized type, subdivided into herpetiform, exfoliating bullous and exfoliating pustular; lastly, that of TORRES into the bullous, the chronic or foliaceous, and the cachectic [see this *Bulletin*, 1945, v. 42, 311].

The author proposes a new classification based on the results of blood examination, the clinical course and the histopathology of the skin lesions—a mingling of those cited above. The blood differences are given in a protocol of the averages of 16 *formes frustes* and 314 generalized cases. These differences are not great, the main being a higher eosinophilia in the latter, 14·8 per cent. as compared with 10·46 in a total leucocyte count of 10,469 and 9,282 respectively, and a differing "nuclear deviation" [? Arneth index], 1/22·5 in the *formes frustes*, 1/14·6 in the generalized type. The histology of the skin in the acute bullous phase, the chronic, the cachectic and retrogressive phases are well shown in a series of photomicrographs, and photographs of patients depict the clinical variations. The chronic phase, the author states, may be further subdivided into foliaceous, erythrodermic and pigmentary forms.

H. Harold Scott

FONZARI, M. Doses de metoquina no tratamento do pênfigo foliáceo. [**The Dosage of Metoquine [Atebrin] in the Treatment of** *Pemphigus foliaceus*.] *Arquivos de Dermat. et Sifiligrafia de São Paulo*. 1947, Mar.–June, v. 11, Nos. 1/2, 17–28. English summary.

There has been considerable conflict of opinion as to the dosage of atebrin and the length of time for which it can be given with safety, and what intervals should be interspersed when courses of it are administered.

The author has tried it in a large number of cases of *pemphigus foliaceus*. He started with 0·2 gm. daily for a week, then, after the lapse of 4 days, repeated the course. Observing no ill effects, he tentatively increased the dose first to 0·3 gm., then to 0·4 and so on, even up to 1·0 gm. and maintained it for several weeks, even months, and rarely did he observe untoward symptoms. One man, having had 0·2 gm. daily, then 0·3 and finally 0·4 gm. till he had had in all 29·4 gm. did develop a "toxic psychosis" [not described]. Brief notes—a couple of lines or so to each—are given of 50–60 cases; several were given 80–90 gm. in 7 months and one had 110·8 gm. in 9 months. Some patients cleared up on this treatment, but commonly a few lesions remained, especially on the legs, and after cessation of treatment these might retrogress. It would appear that when the condition had so far improved as to leave only these few lesions, further treatment with atebrin was ineffectual. The best results were observed in those who exhibited marked yellowing of the skin; this staining is not to be regarded as a toxic symptom and it clears up in time, whether treatment is continued or not. Other drugs such as paludrine and plasmoquine were tried but were quite ineffectual in this disease.

H. Harold Scott

BASSET, A., COLDEFY & DE KOUROCH. Trois cas parisiens de pied de Madura dus à une mycose (famille des "Aspergillacées"). [**Three Cases of Madura Foot in Paris due to an Organism of the** *Aspergillacea* **Family.**] *Bull. Acad. Nat. Méd.* 1948, v. 132, Nos. 1/2, 41–4. 1948

DOSTROVSKY, A. & SAGHER, F. **Failure of Sulphonamides and Penicillin in Maduromycosis.** *Lancet*. 1948, Jan. 31, 177–8, 2 figs. [15 refs.]

The authors note that little attention has been paid to the effect of sulphonamides or penicillin on deep mycoses of the skin: such references as are quoted refer largely to actinomycotic lesions, and such a one, in a case of Madura

foot, is referred to by PETERS [this *Bulletin*, 1946, v. 43, 246]. In Peters's case, 1,050,000 units of penicillin were given without specific effect.

The case described by the present authors was one of maduromycosis in a native of Aden. Colonies of a madurella type were found on culture and these resembled *Madurella americana*. Intracutaneous tests with tricophytin and with material from cultures of the lesion were negative. Therapy which included sulphapyridine (total dosage 72 gm.) brought about improvement, but not healing. Three and a half years later the patient was seen again, and there was now considerable involvement of the bones of the foot. Thereapy included sulphadiazine (total dosage 100 gm.) and X-rays. As this was without effect, sodium penicillin was given in intramuscular doses of 10,000 to 15,000 units every 3 or 4 hours to a daily total of 90,000 units ; in addition, injections of 10,000 units were given locally into the tumour. In 50 days a total of 5,000,000 units of penicillin was given. Secondary infection was overcome, but the mycetoma did not respond and the foot was therefore amputated.

Practical difficulties made it impossible to test the sensitivity of the fungus to penicillin *in vitro*. The authors believe that the failure of penicillin may be explained by (1) insensitivity of the fungus, (2) insufficient dosage, (3) inadequate contact between the penicillin and the fungus, because of the depth in the bone to which the mycetoma had penetrated.

H. J. O'D. Burke-Gaffney

FRIESS & DELVOYE. A propos d'un aspect chirurgical d'une mycose rare ; histoplasmose. [**Concerning a Surgical Aspect of a Rare Mycosis ; Histoplasmosis.**] *Cahiers Méd. Union Française.* Algiers. 1947, June, v. 2, No. 11, 419–25, 8 figs.

The authors describe a fatal case of histoplasmosis, of an unusual pathological type, in a native of Senegal, in which the lesions occurred chiefly in the osseous and cutaneous systems. The upper cervical vertebrae were extensively damaged and a resulting cold abscess, pointing in the posterior triangle of the neck, prompted the diagnosis of Pott's caries of the cervical spine. "Gummatous" lesions, in which the large parasitic form of *Histoplasma capsulatum*, measuring up to 12μ in diameter, was found, occurred in the frontal and maxillary bones, the femur, the tibia and the bones of the forearm. *H. capsulatum* was cultivated from the lesions before and after death. The skin over the greater part of the body was thickened, dry and cracked in places, and miliary ulcers were scattered on the face and limbs. Histological examination of the skin revealed hyperacanthosis of the epidermis with giant-cell granulomata, rich in *Histoplasma*, in the cutis. Outstanding pathological features of this case were the unusual distribution of the lesions with apparently no involvement of the lymph nodes or the lungs and only minor involvement of the liver and spleen.

[This is only the fifth reported case of histoplasmosis from tropical and northern Africa : the other four were, two diagnosed by the reviewer in 1943 and 1946, one by CATANEI & KERVRAN in 1945 [this *Bulletin*, 1946, v. 43, 247] and one by KERVRAN & ARETAS in 1947 [*ibid.*, 1948, v. 45, 207]. In all, the parasite was of an unusually large size, measuring from 12 to 15 μ in longer diameter, which suggests that there is a distinct African variety of *Histoplasma capsulatum*.]

J. T. Duncan

MILLER, H. E., KEDDIE, Frances M., JOHNSTONE, H. G. & BOSTICK, W. L. **Histoplasmosis : Cutaneous and Mucomembranous Lesions, Mycologic and Pathologic Observations.** *Arch. Dermat. & Syph.* 1947, Dec., v. 56, No. 6, 715–37, 3 figs. [Refs. in footnotes.]

This is a general account of histoplasmosis, compiled from the recent literature, in which emphasis is specially placed on the mucosal and cutaneous lesions

which are of interest to dermatologists. The authors also describe, at great length, the clinical and pathological features of a case of this disease in which the only ascertained lesion of histoplasmosis was an ulcerating nodule, 1·5 cm. in diameter, on the dorsal aspect of the tongue. The diagnosis was based on the identification of *Histoplasma capsulatum* in scrapings from the ulcer and on the isolation of the fungus from this material. There was general lymphadenopathy and some enlargement of the liver, but not of the spleen, A few bodies which may have been *Histoplasma* were seen in some of the cervical lymph nodes, but, on the whole, the microscopical examination of the lymph nodes yielded data more suggestive of Hodgkin's disease than of histoplasmosis. The final diagnosis, based on the necropsy findings was : generalized miliary tuberculosis, Hodgkin's disease of the malignant lymphoma type and localized histoplasmosis.

[It is noteworthy that cases have been described of histoplasmosis and of torulosis which bore a strong resemblance to Hodgkin's disease, not only in their clinical features but in the histology of the lymph nodes, and there is still uncertainty as to whether these were cases of true Hodgkin's disease with superadded mycosis, or the uncomplicated mycoses simulating Hodgkin's disease.] *J. T. Duncan*

ROSENTHAL, S. R. & ROUTIEN, J. B. **Contagiousness of Coccidioidomycosis. An Experimental Study.** *Arch. Intern. Med.* 1947, Sept., v. 80, No. 3, 343–57, 5 figs. [Refs. in footnotes.]

Infection in coccidioidomycosis is caused by inhalation of the air-borne spores of the saprophytic growth of *Coccidioides immitis*, and the disease is not known to be transmitted directly from man to man. The work recorded in the present paper was designed to explore the possibility of direct transmission of the infection by transference of the parasitic spherules of the fungus. Experimental infection of guineapigs was accomplished by intratracheal insufflation of sputum, pus, ground-up granulation tissue or lymph node material, containing the parasitic spherules, from human sources. The infective material was introduced through a wide-bore syringe needle inserted into a tracheotomy opening, and it was driven into the bronchial tree by air pumped from the syringe. The resulting lesions of coccidioidomycosis were found chiefly in the upper lobes of the lungs. Infection was also effected by intraperitoneal injection of similar materials. As a test of survival of the parasitic form of the fungus outside the body, morbid materials containing the spherules were stored for varying periods at 12°C. These materials were found to be infective to the guineapig by intratracheal insufflation up to 110 days.

From the results of their experiments, the authors conclude that coccidioidomycosis should be considered to be contagious until the contrary is proved.

J. T. Duncan

MCLAUGHLIN, F. W. **Coccidioidal Infection.** *Bull. U.S. Army Med. Dept.* 1948, Feb., v. 8, No. 2, 124–7.

Coccidioidomycosis is endemic in the Camp Roberts area in California and since the inception of the U.S. Army Hospital there in 1941, over 750 cases of *C. immitis* infection have been confirmed [this *Bulletin*, 1946, v. 43, 778].

The present author reviews 20 of these cases and notes that the usual symptoms were chest pain (20), fever (18) and cough (15). The commonest signs were X-ray evidence of pulmonary infiltration (20), increased sedimentation rate (12) and leucocytosis (8). Hilar adenopathy and pleural effusion were each seen once.

It is noteworthy that only 4 of the cases had positive skin tests and the author stresses the point that these tests are negative in many active cases of

coccidioidomycosis. Skin tests may, however, become positive very rapidly and a detailed account is given of one patient on whom such a test was positive at 1/1,000 on the fifth day after mild symptoms were noticed. On the other hand, complement-fixation and precipitin tests do not always become positive early: a case is quoted of a patient having X-ray evidence of a chest lesion and showing a positive skin test at 1/1,000, but whose complement-fixation did not appear for over 3 weeks.

The two serological tests are usually necessary for final diagnosis, since lesions seen in chest films so closely resembled those of tuberculosis: in many cases, skin tests for tuberculosis and for coccidioidomycosis were both positive, and indeed occasionally the two diseases may co-exist.

The best method of diagnosis is probably obtained by culture of sputum and guineapig inoculation, where facilities are available. The author found the raised sedimentation level to be fairly frequent [the figure of 60 per cent. is given, but the numbers were only 12 out of 20]. He also believes the sedimentation rate to be of prognostic significance, especially since its return to normal tends to correspond with X-ray evidence of clearing. It is suggested that the sedimentation level is an important factor in determining when a patient may become ambulatory (as in the case of rheumatic fever).

No specific therapy was found and penicillin and sulphonamides proved ineffective. Treatment was largely a matter of general principles and good nursing. *H. J. O'D. Burke-Gaffney*

MISCELLANEOUS DISEASES

RAYMOND, W. D. **Notes on a Poisonous East African Species of Wild Cucumber** (*Cucumis aculeatus*). *East African Med. J.* 1947, Dec., v. 24, No. 12, 450–51.

The toxicity of a number of species of wild cucumber has been investigated in South Africa; it has been shown that *Cucumis africanus* and other species contain a toxic principle, cucumin, which is neither a glycoside nor an alkaloid. In human poisoning, violent diarrhoea has been noted. In laboratory animals, postmortem appearances varied with the dose: with small doses, the gastro-intestinal tract was principally affected: with large doses, pulmonary oedema was the usual cause of death.

The author describes a fatal case of poisoning of an African in Tanganyika who was treated for headache by a local "medicine-man" with the fruit of a plant *Kisawasawa*: this was identified as *Cucumis aculeatus*. Vomiting and diarrhoea occurred soon after the medicine was taken. Death took place within 8 hours and although the passage of time during transport obscured the autopsy findings, pleural adhesions were noted.

From the fruits a substance was isolated which gave reactions similar to those described for cucumin: it is highly probable that the fruit contains a substance closely related to, if not identical with, cucumin.

The substance isolated and fresh extracts of the fruit were lethal, within 1 to 6 hours, to a mouse, two white rats and a frog, on injection. In the rats and the mouse, dyspnoea and cyanosis were noted and the pathological findings in the lungs at postmortem showed that they had "the appearance one would find in acute pulmonary oedema."

Other local species of *Cucumis* known to be poisonous are *C. africanus*, *C. ficifolius* and *C. hirsutus*; poisoning has also occurred from other species not exactly identified botanically. *H. J. O'D. Burke-Gaffney*

DONOSO BARROS, R. Myiasis humana en Chile. Consideraciones clinicas y epidemiologicas. **[Human Myiasis in Chile. Clinical and Epidemiological Features.]** *Rev. Chilena de Hig. y Med. Preventiva.* 1947, Mar., v. 9, No. 1, 3–59, 3 figs. & 10 pls. [83 refs.]

The author bases his remarks on 112 cases of human myiasis under his personal observation during the five years ending 1946. The numbers in successive years were 1, 2, 7, 17 and 85; 7 were under 5 years of age, 10 each between 36 and 40, and 46 and 50 years. His own observations are supplemented by references to and quotations from the literature and there is a very full bibliography. The author divides his cases into two main groups: Myiasis of cavities (*i.e.*, orifices), nasal, aural, ocular, vulvovaginal and intestinal (including the mouth). The second group is that of cutaneous myiasis, attacking the unbroken skin or lesions such as ulcers, wounds, etc. The following larvae were identified: *Cochliomyia hominivorax*, *Calliphora erythrocephala*, *Musca domestica*, *Musca chilensis*, *Fannia canicularis*, *Eristalsis tenax*, *Oestrus ovis*, *Gastrophilus veterinus*, *Sarcophaga carnaria* and *Parasarcophaga barbata* [*Sarcophaga barbata*]. In previous accounts *C. macellaria* has been named as causing myiasis in Chile, but this, it is stated, was a mistake for *C. hominivorax* [though some authors use the names as synonyms.] *H. Harold Scott*

MILLER, J. M. & THOMISON, S. J. **Surgical Aspect of Infestation with Intestinal Parasites.** *Southern Med. J.* 1948, Feb., v. 41, No. 2, 178–80.

"Case reports of patients with Enterobius vermicularis, Schistosoma japonicum, hookworm, and amebiasis have been presented. The discovery of parasites in patients with otherwise unexplained abdominal symptoms will remove this group of individuals from those with the unsatisfactory diagnosis, 'abdominal pain, cause undetermined'. The surgeon is urged to familiarize himself at least superficially with these parasites, that he may consider them in his differential diagnosis of unusual abdominal pain."

PROTOZOOLOGY: GENERAL

APPELBAUM, A. **Human Toxoplasmosis. Report of a Case in an Adult with Ocular Manifestations.** *Ann. Western Med. & Surgery.* 1947, Oct., v. 1, No. 8, 323–32. [27 refs.]

The paper describes a case of toxoplasmosis in a white man 30 years of age and gives a general summary of the literature of the subject. The case in question was examined because of the patient's complaint of blurred vision of the left eye; a small patch of chorio-retinal atrophy was found just temporal to the fovea centralis, together with a small recent haemorrhage between the patch and the fovea centralis. Two years later the patient was again examined and he now revealed a bilateral central chorio-retinitis. The lesion in the left eye had increased in size and showed a black pigmented centre and a zone of peripheral pigment. In addition, two other small lesions had appeared. As toxoplasmosis was suspected, a serological test for neutralizing antibodies was carried out. This was positive. Cerebrospinal fluid injected into mice did not give rise to infection. The author points out that this case is the forty-second to be reported in the U.S.A. since 1939. Of these cases, nine occurred in persons over 15 years of age. *C. M. Wenyon*

KEAN, B. H. & GROCOTT, R. G. **Asymptomatic Toxoplasmosis.** *Amer. J. Trop. Med.* 1947, Nov., v. 27, No. 6, 745–8, 1 fig. [17 refs.]

A man 29 years of age died from an accident, and examination of sections of the heart muscles revealed a cyst measuring 54 by 96 μ. It was filled with spores, 250 being countable in the section. There was no inflammatory reaction round the cyst. Extensive examination of further sections from the heart and other organs failed to reveal any other parasites. It is thought that the cyst shown in a microphotograph represents a toxoplasma. *C. M. Wenyon*

ENTOMOLOGY AND INSECTICIDES: GENERAL

LUMSDEN, W. H. R. **Observations on the Effect of Microclimate on biting by *Aëdes aegypti* (L.) (Dipt., culicid.).** *J. Exper. Biol.* 1947, Dec., v. 24, Nos. 3/4, 361–73, 2 figs. [20 refs.]

The mosquitoes were reared under carefully controlled conditions, and were offered a blood meal in a small cage applied to the human arm in darkness. It was found that wide variations of the relative humidity did not appreciably affect the proportion biting, which rose from about 10–20 per cent. at 10°C. to a maximum of 90 per cent. (within five minutes) at 35°C. Only about 60–70 per cent. fed at 40°C. Measurements of temperature gradients near the human skin were made with a sensitive electrical thermometer. At air temperatures below that of the skin, the gradient extended away for only about 1 cm. in nearly still air. At air temperatures above the skin there was a gentle reversed gradient for 2–3 cm. It seems unlikely that these gradients can be responsible for attracting mosquitoes to bite, especially when the air temperature is above that of the skin.

Dissections showed that in the majority of fed mosquitoes, blood was found in the stomach alone; but in partly fed mosquitoes there was a somewhat larger minority with blood in the diverticula also, probably because of regurgitation when feeding was interrupted. *J. R. Busvine*

PARROT, L. & DURAND-DELACRE, R. Notes sur les phlébotomes. LVII. Présence en Algérie de *Phlebotomus clydei* Sinton, 1928. [**Notes on *Phlebotomus* LVII. Presence of *Phlebotomus clydei* Sinton in Algeria.**] *Arch. Inst. Pasteur d'Algérie.* 1947, Sept.–Dec., v. 25, Nos. 3/4, 210–11.

SWELLENGREBEL, N. H., LODENS, J. G. & SWELLENGREBEL, J. M. H. Rapport over proeven nopens beschilderen van indonesische woningen met D.D.T. in Tjiandjoer en omgeving. [**Trial of DDT "Paint Spraying" of Indonesian Dwellings.**] *Med. Maandblad.* Batavia. 1947, Dec., No. 17, 319–25.

SCHMITZ, W. R. & GOETTE, Mary B. **Penetration of DDT into Wood Surfaces.** *Soap.* New York. 1948, Jan., v. 24, No. 1, 118–21, 2 figs.

Two types of DDT spray were used: kerosene solutions, and aqueous emulsions of DDT dissolved in various solvents. The liquids were carefully sprayed on to strips of wood with an atomizer and the penetration was subsequently judged by extraction and chemical (colorimetric) estimation of DDT from layers scraped off the surface. The thicknesses of the layers scraped off were estimated by average micrometer measurements.

The authors used a variety of woods, and the average recovery of DDT (kerosene solutions) from the first 0·001 inch was 25 per cent., and from the

first 0·006 inch 52 per cent., of the amount theoretically applied. Equivalent figures for emulsions, were 37 and 70 per cent. respectively. At depths below 0·006 inch the amounts in different layers fell away asymptotically. (Thus, at 0·04 inch the quantities recovered were still only 65–85 per cent.)

There was little evidence of correlation between the physical properties of the different woods and the recovery of DDT from the upper layers. Preliminary spraying of wood with water did not greatly improve DDT recovery if the DDT liquid was sprayed on immediately afterwards ; but there was definite improvement after one spraying with water and drying for fifteen minutes before application of the DDT.

Tests with different solvents in the emulsion formula suggested that the more volatile DDT solvents tended to leave more DDT near the surface.

J. R. Busvine

SMITH, M. S. **Persistence of D.D.T. and Benzene Hexachloride in Soil.** [Correspondence.] *Nature.* 1948, Feb. 14, 246.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

BULL. MÉD. DE L'AFRIQUE OCCIDENTALE FRANÇAISE. 1946, v. 3, No. 2, 271–84. L'actualité médicale dans l'Ouest Africain. Conference médicale Franco-Britannique d'Accra—Novembre 1946. [**Franco-British Medical Conference, Accra, 1946.**]

The agreements reached at this Conference are set out *seriatim.* They cover :— A. Cooperation between health services in the various countries of West Africa, and proposals for coordination of medical action ; B. Agreements relating to the medical instruction of Africans ; C. Facilities for the diagnosis of yellow fever (the accredited laboratories are at Dakar, Freetown, Accra, Lagos, Douala, Stanleyville, Brazzaville) ; D. Preparation and distribution of vaccines for mutal assistance ; E. Collaboration in studies of nutrition ; F. General principles of closer cooperation between the various countries ; G. Final recommendations, in which it is noted that Belgian and other representatives agreed to the principal resolutions.

There are three Annexures, dealing respectively with mobile medical organizations, schedules of instruction for Africans, and the organizations interested in nutrition.

No adequate summary of this Conference can be given ; the resolutions are given with little comment, and should be studied in the original. There is evidence of a desire to improve inter-territorial medical collaboration.

Charles Wilcocks

MALAYA. **Annual Report of the Institute for Medical Research, Malaya, for the Year 1946** [LEWTHWAITE, R., Director]. 52 pp. 1947. Kuala Lumpur : Malayan Union Govt. Press. [$1 or 2s. 4d.]

In the introductory part of this Report, Lewthwaite briefly traces the history of the Institute since its foundation in 1900. He gives an account of the action taken just before the Japanese occupation, and, in more detail, after the capitulation of the Japanese in 1945. The loss of equipment during the occupation was almost complete, and the laboratories were re-equipped from whatever sources could be tapped.

The demand for vaccines after the war was very great, and was met with difficulty; supplies were also needed for Siam and Borneo.

The author pays tribute to his colleagues not only for their scientific work in peace, but also for their service in war; several lost their lives, and many of them suffered severely.

Work is now continuing, as routine investigation or special research, in the Divisions of Bacteriology, Chemistry, Entomology, Malaria Research, Nutrition, Pathology and Serology, and the branch laboratory at Ipoh is once more functioning. Records of these activities are displayed in the report.

Charles Wilcocks

NEW ZEALAND: WESTERN SAMOA. **Twenty-Fourth Report of the Administration of the Territory of Western Samoa for Year ended 31st March, 1947** [VOELCKER, F. W.]. 27 pp. Wellington: Govt. Printer.

Western Samoa comprises two large and several small, mountainous, islands. The climate is mild and equable, the mean daily maximum temperature being 84·75°F., minimum 73·82°F., and the average annual rainfall 111 inches. The population consists of 5,765 non-Samoans, and 65,695 Samoans; most of the latter live in coastal villages. The islands are administered by the Government of New Zealand under the international trusteeship system of the United Nations, but their status is under review.

The medical section of this Report (p. 19–23) is brief. The staff consists of 3 European medical officers, 22 Native medical practitioners, 7 Native dental officers, 1 qualified bacteriologist of part-Samoan descent, 11 European nursing sisters, 97 Native nurses, and others. There is a considerable hospital at Apia, which accommodates Europeans, Samoans and Chinese, and includes a laboratory and X-ray department. There are 13 medical out-stations, to each of which a Native medical practitioner and nurse are attached. At all stations, in 1946, there were 3,631 in-patients, and 99,104 out-patients.

The principal infective diseases reported in 1946 were tuberculosis (48 cases), malignant jaundice [not otherwise defined] (71), catarrhal jaundice (93), pneumonia (244), bronchopneumonia (73) and enteric fever (37). The tuberculosis situation was investigated by Dr. C. A. TAYLOR of New Zealand, who concluded that it was not particularly serious.

The infant mortality rate was 106 per 1,000 registered births in 1926, 291·77 in 1936 (the high figure was the result of epidemics of whooping cough and measles) and 64·05 in 1946.

Charles Wilcocks

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ALPHABETICAL LIST OF AUTHORS OR SOURCES

Andrews, J. C. & Cornatzer, W. E., 396.
Appelbaum, A., 469.
Augustine, D. L., 417.
Azulay, R. D., 440.

Baltazard, M., Bahmanyar, M. & Mofidi, C., 434.
Bassères, M. S. & Pantoja, W. P., (443).
Basset, A., Coldefy & de Kouroch, (465).
Becmeur, A., 450.
Bertazzi, C. G., (423).
Bettinardi, G., 423.
Biraud, Y. & Kaul, P. M., 426.
Bodman, R. I. & Stewart, I. S., 433.
Boshes, B., 396.
Boyd, M. F., 395.
—— & Kitchen, S. F., 393.
Braga, E., Penido, H. M., Bassères, M. S., Pinto, D. B., Bezerra, F. P., Jr. & Moura, F. P., 408.
Bull. Méd. de l'Afrique Occidentale Française, 471.
Bull. World Health Organization, 389.
Buonomini, G. & Motta-Diana, A., 399.

Caldwell, F. E. & György, P., 417.
Carnevale, A., 419.
Causey, O. R., Costa, O. & Causey, C. E., (443).
Chen, G., 397.
Cole, L. C. & Koepke, J. A., 421
Conan, N. J., Jr., 430.
Contreras Duenas, F., (436).
da Costa, O. R., (443).
Cowan, G. A. B., 463.
Covell, G., (401).
Cowper, S. G., 444.
Curd, F. H. S., Graham, W., Richardson, D. N. & Rose, F. L., (401).

Darby, W. J., Jones, E., Warden, H. F. & Kaser, M. M., 461.
Davidson, A. G., Baron, B. & Walzer, M., 452.
Deane, M. P., 417, 435.
Dearborn, E. H., 397.
Donoso Barros, R., 469.
Dore, G. M., (418).
Dostrovsky, A. & Sagher, F., 465.
Douglas, B., Jacomb, R. G. & Kermack, W. O., (401).
Dubois, A., 436, 438.

Eeraerts, W., 412.
Erzin, N. & Payzin, S., 426.

Faget, G. H. & Erickson, P. T., 442.
Faust, E. C., 426.
Ferola, R., (443).
Fite, G. L., Erickson, P. T., Gemar, F. & Johansen, F. A., 442.
Floch, H., 437.
—— & Camain, R., (442).
Fonzari, M., 465.
Fourman, L. P. R., 460.
Franks, M. B., Chenoweth, B. M., Jr. & Stoll, N. R., 453.
Friess & Delvoye, 466.
Fulton, J. D. & Joyner, L. P., 430.

Gallut, J. & Grabar, P., 427.
Gatto, I., 418.
Gaud, M., Khalil Bey, M. & Vaucel, M., 432.
—— & Morgan, M. T., 431.
Gelfand, M., 411.
Girgis, B. & Aziz, S., 446.
Giroud, P., 420.

Glusman, M., (459).
Gramiccia, G. & Saccà, G., 408.
Guideri, G., 418.

Hadler, W. A., 464.
Hanafy, M., 458.
Harding, R. D. & Hutchinson, M. P., 410.
Hauschka, T. S., 415.
Hawking, F., 388.
Hewitt, R. I., Kushner, S., Stewart, H. W., White, E., Wallace, W. S. & SubbaRow, Y., 455.
——, Wallace, W. S., White, E. & SubbaRow, Y., 454.
——, White, E., Wallace, W. S., Stewart, H. W., Kushner, S. & SubbaRow, Y., 455.
Hirvonen, M., 450.
Ho, T. T., 459.
van Hoof, L., Henrard, C. & Peel, E., 412.
——, ——, —— & Wanson, M., 456.

Internat. J. Leprosy, (436).

Kailin, E. W., Davidson, A. G. & Walzer, M., 452 *bis*.
Kean, B. H. & Grocott, R. G., 470.
Kervran, P., 445 *bis*.
Kierland, R. R. & McCreight, W. G., 400.
Kirk, R., 424.
Kubicz, J., 420.

Lara, C. B., (437).
Lauterburg-Bonjour, M., 393.
Lewthwaite, R., 471.
Lumsden, W. H. R., 470.
Luttermoser, G. W., 447.

McLaughlin, F. W., 467.
Makari, J. G., 394, 395.
Malaya, 471.
Manson-Bahr, P. & Muggleton, W. J., 429.
Mauzé, J., 390.
Mellinkoff, S. M. & Higgins, J. R., 396.
Mendes, P. & Mangeon, G., (438).
Miller, H. E., Keddie, F. M., Johnstone, H. G. & Bostick, W. L., 406.
Miller, J. M. & Thomison, S. J., 469.
Mondini, E. M., (418).
Montoya, J. A., Osejo, P. P. & Topping, N. H., 419.
Muniz, J. & de Azevedo, A. P., 416.
Murano, G., 418, (419).

Ness, A. T., Brady, F. J., Cowie, D. B. & Lawton, A. H., 447.
New Zealand, 472.

Pantoja, W. P. & Bassères, M. S., 451.
Parrot, L. & Durand-Delacre, R., (470).
Penido, H. M., 391.
——, Azevedo, N., Pinto, D. B., Bezerra, F., Jr., de Sousa, E. F. & Moura, F. P., 408.
Perk, D., 398.
Philip, C. B., 424.
Pinto, G. de S., 400.
Porritt, R. J. & Olsen, R. E., 441
Portugal, H., 439.

Raymond, W. D., 468.
Rees, C. W. & Reardon, L. V., 428.
Reeves, D. L. & Kerr, R. W., 448.
Remlinger, P. & Bailly, J., 387.
Rigdon, R. H. & McCain, B. E., 409.

[*Continued overleaf*

ALPHABETICAL LIST OF AUTHORS OR SOURCES—*cont. from page 3*

Risi, J. B., 438.
Rodriguez, J. N., 439.
Román P., J., 415.
Rosenthal, S. R. & Routien, J. B., 467.
Ross, H., (442).
Roumagoux, J., (419).
Roy, H. K. & Bhattacharjee, R. C., (419).

Salle, L., 432.
Scheifley, C. H., 395.
Schmitz, W. R. & Goette, M. B., 470.
Schujman, S., 441.
Schwetz, J., 392.
Sergent, Et., 463, 464.
Shortt, H. E. & Garnham, P. C. C., 388.
——, —— & Malamos, B., 388.
Smadel, J. E., Snyder, M. J. & Robbins, F. C., 424.
Smith, M. S., (471).
de Souza-Araujo, H. C., (436), (441).
de Souza Lima, M., Barba Rubio, J., de Souza Lima, L. & Rath de Souza, P., 440.
Soysa, E., 395.
Spadaro, O., 390.
Spies, T. D., Garcia Lopez, G., Stone, R. E., Milanes, F., Brandenburg, R. O. & Aramburu, T., 460.
——, ——, ——, ——, Toca, R. L. & Aramburu, T., 462.
Spingarn, C. L. & Edelman, M. H., 428.
Stryker, W. A., 457.
Swellengrebel, N. H., Lodens, J. G. & Swellengrebel, J. M. H., (470).

Thomson, R. C. M., 405.
Tonkin, I. M. & Hawking, F., 409.
Totterman, G., 449.
Trager, W., 393.
Tuna, I., 421.

Valls, D. J., 416.
Vanbreuseghem, R., 434.
Vanderplank, F. L., 413.
Vertiainen, I. & Bastman-Heiskanen, L., 449.
Voelcker, F. W., 472.

Walton, G. A., 401.
Wanson, M., Richard, P. & Toubac, M., 425.
——, Wolfs, J. & Lebied, B., 392.
Wharton, L. H., 442.
Wilde, J. K. H., 414.
Wiley, J. S., 423.
Wilkins, A. J. W., 443.
Williamson, J. & Lourie, E. M., 413.
Wolfs, J., 392.
Wolstenholme, B. & Gear, J. H. S., 434.
Wright, A. W. & Coombes, A. E. R., 423.

Ybarra Pérez, R. & González Prendes, M. A., 437.

Zito, P., 444.

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